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ANNALS OF
INTERNAL MEDICINE

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A COMMON LESION OF THE CERVICAL SPINE RESPONSIBLE FOR SEGMENTAL NEURITIS *

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VON BECHTEREW,[1] Strümpell,[2] and Marie [3] described many years ago some of the neurological problems associated with arthritic changes in the vertebral column. These early investigators observed variable clinical pictures in their cases of spinal arthritis and frequently found that there was no direct relationship between the arthritic change and the intensity of the neurological symptoms. Spastic, atrophic, or hypertonic motor changes and irritative sensory phenomena, or occasionally anesthesia and flaccid paralysis were present in certain of their cases with arthritic changes in the vertebral column.

In 1916 Nathan,[4] who had observed numerous cases of spinal arthritis with neurological symptoms, induced experimental non-suppurative arthritis in animals in order to study the relationship between the pathological changes and the resulting symptomatology. Evidences were obtained of thickening of the periosteum of the vertebrae, thickening of the connective tissue in the region of the costo-vertebral joints and epidural exudate infiltrating the epidural areolar spaces. It was felt that these changes could lead to irritation and compression of nerve roots, the symptomatology depending upon the degree of nerve root involvement.

Williams and Yglesias [5] studied the lumbar spine of a large number of cases suffering from sciatica and demonstrated a rupture of the nucleus pulposus with resulting collapse of the intervertebral disc and narrowing of the space between the fifth lumbar vertebra and the sacrum. Schmorl [6] had previously described these findings in his studies of autopsied material. This condition caused a subluxation of the facets and a constriction of the intervertebral foramina. Subsequent irritation and compression of the fifth lumbar nerve roots produced the painful symptomatology observed in these cases.

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In 1934 Nachlas [7] described a syndrome of pseudo-angina pectoris originating from demonstrable changes in the cervical spine. Each of the three cases described by him had a definite arthritic involvement of the lower cervical spine associated with thoracic pain. Irritation and compression of the cervical nerve roots secondary to these arthritic changes was felt to be the cause of the referred pain along the medial anterior thoracic and lateral anterior thoracic nerves. These nerves are motor pathways and supply the pectoralis major and minor muscles. Nachlas noticed that acute hyperextension and lateral bending of the neck produced a stab of pain referred to the region beneath the scapula or in the precordium of his patients.

Hanflig [8] has recently described a group of 30 cases of pain in the shoulder girdle, arm and precordium due to cervical arthritis. He noted certain relatively characteristic clinical features of arthritis of the cervical spine, of which he placed rigidity and pain as the two most outstanding symptoms. He described these cases as frequent and as representing a large group of elderly individuals with symptoms commonly classed as neuritis. A successful method of treatment by traction and manipulation of the neck had been used on his patients.

This paper deals with a critical survey of over 50 patients observed by the authors during the past four years. It is presented because of the presence of a common finding in the cervical spine consisting of a distinct and clear cut narrowing of one or more of the intervertebral spaces.

Most of the patients in this group were over 50 years of age although two patients only 27 years old are included.

Pain in some part of the shoulder girdle, arm, hand, back, precordium or neck was usually the chief complaint though a few cases gave muscular weakness or inability to perform certain normal movements of the upper extremity as the most troublesome symptom. The pain described by patients was quite variable in degree and type. Some complained only of paresthesias while others experienced severe radiating pains. The location and types of pain observed in this group are outlined below.

1. Pain in one or both shoulders.
2. Pain radiating down the arms (usually unilateral).
3. Pain on the radial side of the forearm and wrist.
4. Tingling sensations in the fingers.
5. Local painful spot between the scapulae.
6. Pain under one scapula.
7. Pain low in the neck (posteriorly).
8. Pain on turning the neck to one side.
9. Precordial distress, diagnosed in several cases as aortitis or angina.
10. Pain exaggerated by walking or riding.
11. Inability to sleep because of pain in the recumbent posture.
12. Pain accompanied by limitation of certain types of movement of the upper extremities.

Pain was usually unilateral although it had shifted from one upper extremity to the other after months or years in several of the cases. In each of the instances where pain had shifted from its original site to the opposite side there has been a residual weakness of the muscles in the previously involved extremity. There was a simultaneous bilateral involvement in only a few of our cases. Most of the patients were not conscious of pain in the neck and, with two exceptions, did not give this as part of the chief complaint. With two exceptions there was no definite restriction of neck movements on passive or active turning of the head and neck in all possible directions. Whenever a patient complained of exaggeration of pain on walking, immediate, and in one case total, relief of this complication was obtained by having the patient wear soft rubber soles and heels. Pain over one shoulder was the most common of all chief complaints. Most of the patients had been suffering for months or years and had been subjected to various treatments. The story usually included a diagnosis of arthritis in the shoulder and treatment had been directed towards relief of the symptoms in that region. Salicylates had been used in some form by all of these patients. Only passing relief or no relief at all had been obtained from the use of salicylates. Some had been subjected to almost every conceivable form of treatment including ultra-violet light, diathermy, other forms of dry and moist heat, deep roentgen-ray therapy, ointments, liniments, massage and even cautery over the shoulder. Several patients had been treated for elevated blood uric acid because of a " uric acid diathesis." Unfortunately we found that no blood studies had been made on such cases prior to the use of cinchophen and allied substances. Blood studies in our laboratories in these patients failed to reveal an abnormal uric acid level. Obtaining little or no relief, these patients had become " medical drifters " going from one physician to another, even visiting the village cautery expert or some other irregular healer in an attempt to gain aid.

Next to pain the most common chief complaint was weakness in one upper extremity or an inability to perform certain normal movements. In some instances these disturbed movements were undoubtedly secondary to the pain elicited and were associated with some spasticity. In other cases they were the result of actual atrophic changes. Several patients complained of difficulty in writing. One patient, a nurse, found that she could no longer hold her pen properly and that it would slip from between her thumb and index finger when she started to write. In both male and female patients we observed numerous instances of inability to raise the arm in the type of movement involved in brushing or combing the hair. Placing a hat on or removing it from the head was a difficult procedure in some instances. Several women encountered great difficulty in fastening the buttons in the back of their dresses. In one instance a physician had difficulty in writing and in grasping the steering wheel of his automobile. The majority of these patients were unable to elevate the hand above the head in the position of abduction of the arm as in the Fascist salute. With two exceptions there

was no restriction of active or passive neck movements. Furthermore there was no observable limitation of movements of the cervical spine, when compared to normal individuals, on roentgen-ray examination in different positions.

Atrophy of the small muscles of the hand has been present in some instances. The hands of these patients may suggest an amyotrophic lateral sclerosis, syringomyelia or progressive muscular atrophy if both sides are involved. When the atrophy is unilateral the condition is suggestive of an accessory cervical rib—a possibility which can easily be eliminated during the roentgenologic study.

Although the types of spinal changes observed roentgenologically have been variable there has been one consistent finding in all of our cases. This has consisted of a narrowing of one or more of the intervertebral spaces in the cervical spine. If neurological symptoms existed in the patient and directed us towards examinations of the cervical spine this narrowing of one or more interspaces was found present regardless of whether we were dealing in addition with hypertrophic arthritis, infectious arthritis or with a traumatic displacement. Furthermore by a special technic developed by one of the authors (Oppenheimer) it was possible to demonstrate by roentgen examination an accompanying narrowing of the intervertebral foramen at the same levels. (The roentgen technic involved is being described in a separate paper.) This narrowing of the interspaces was present in some cases in which there was no roentgenological evidence of "spicule" or exostosis formation. In numerous instances marked hypertrophic changes, such as marginal lipping of the vertebral bodies, were present but the narrowing of the intervertebral spaces also existed. These hypertrophic changes when present always involved the vertebral bodies on either side of a narrowed intervertebral space. One case, a young woman teacher 27 years of age with pain between the scapulae, showed arthritic changes between the fourth and fifth cervical vertebrae suggesting infectious arthritis. Another young woman of the same age showed a narrowing of the interspace between the fifth and sixth cervical vertebrae and a slight anterior displacement of the third and fourth cervical vertebrae.

The following case histories are given in some detail in order to illustrate the findings observed in this group of cases.

Case Histories

Case 1. V. D., a woman, 76 years of age. Complained of marked pain in the left shoulder with weakness of the right arm. The pains were greatly increased on walking or riding in a car. According to her statement pain began first in the right thumb about 17 years ago. This was followed by a dull pain in the whole right arm with definite limitation of movement so that it became difficult for her to comb her hair or to button her dresses at her back. The pain in the right arm gradually subsided after some years but never completely disappeared. Limitation of movement and residual weakness persisted in spite of this relief from pain. Seven months ago her left arm and shoulder became painful. Pain then increased in both shoulders

and arms and eventually became so severe on the left side that she was unable to sleep comfortably. She experienced the greatest discomfort when lying on her back and soon learned that relief could be obtained by placing pillows under the head and bending the neck acutely forward. Marked weakness similar to that previously observed in the right arm began to develop in the left upper extremity. Combing the hair became so difficult that she had her hair cut off short to avoid the necessity of raising the arms to the head. The pain in the arms was invariably increased by walking or riding. When walking, the left arm and shoulder annoyed her so greatly that she developed the habit of holding the left hand in the right to protect the arm against undue movement. She had resorted to innumerable forms of treatment such as diathermy, hot compresses over the shoulder, liniments, ointments, massage locally and salicylates internally without relief.

Physical examination revealed no limitation of passive movement in the shoulder joints. She could not internally rotate the left arm and place the hand behind her back without eliciting marked discomfort. Elevation of the arm in abduction was impossible with either the right or left upper extremity. There was no atrophy of the shoulder girdle, arm or hand muscles. Passive and active movements of the neck were not limited and were not painful. There was no rigidity of the neck musculature.

Roentgen findings revealed that the intervertebral spaces between the fifth and sixth and sixth and seventh cervical vertebrae were definitely narrowed. There was a slight increase in bony density seen in the surfaces of these vertebrae. No exostotic formation, no rarefaction and no deformity of the bodies of the cervical vertebrae were observable. The diseased part was shifted slightly backward. Radiography of the entire spine was then made and no changes similar to those seen in the cervical spine were observed in the lower segments. The body of the twelfth dorsal vertebra was deformed, being flattened in its anterior portion. (Close questioning revealed an old fracture resulting from a fall off a ladder 42 years previously.) Roentgen-rays in different positions revealed no limitation of excursion of vertebral bodies in the cervical region during active movements. (Figure 1.)

It is of special interest in this case to note that the patient observed relief from pain by bending her head forward. This movement relieved the pressure on the nerves in the region of the intervertebral foramen by temporarily widening the foramen. Because her pains were so aggravated on walking she was advised to replace her leather shoe soles with soft rubber soles and heels. This gave remarkable relief immediately from the discomfort on walking. Ultra short wave and deep roentgen-ray therapy over the cervical vertebrae has brought about marked improvement.

Case 2. A. S., nurse, aged 54 years. The chief complaint was pain in both shoulders during the past three months. Her discomfort was most marked in the right shoulder. Certain movements, such as internal rotation of the arm and placing the hand in the middle of the back, caused great discomfort. Fastening a dress with the buttons or hooks in back had become impossible. At times her right shoulder felt quite numb. Three years previously she had noticed weakness in the right hand which was most troublesome when she was holding a pen. The pen would slip from between her thumb and index finger if she attempted to write for any length of time. About a year ago she noticed that the fleshy part of the right hand between the thumb and index finger was becoming shrunken and flat. Recently the pain has been variable in intensity, sometimes radiating down the outer aspect of the right arm. On investigating her history closely it was found that 15 years ago she had had a very sudden attack of severe cervical pain a short time after a fall from horseback. At that time she was unable to turn her head to the left because of pain and it was necessary for a physician to administer several morphine injections for relief.

Examination of the shoulder joints revealed negative findings. Passive movements were free and unrestricted. She could not elevate the right hand above her head with the arm in abduction. She was unable to place the right hand in the

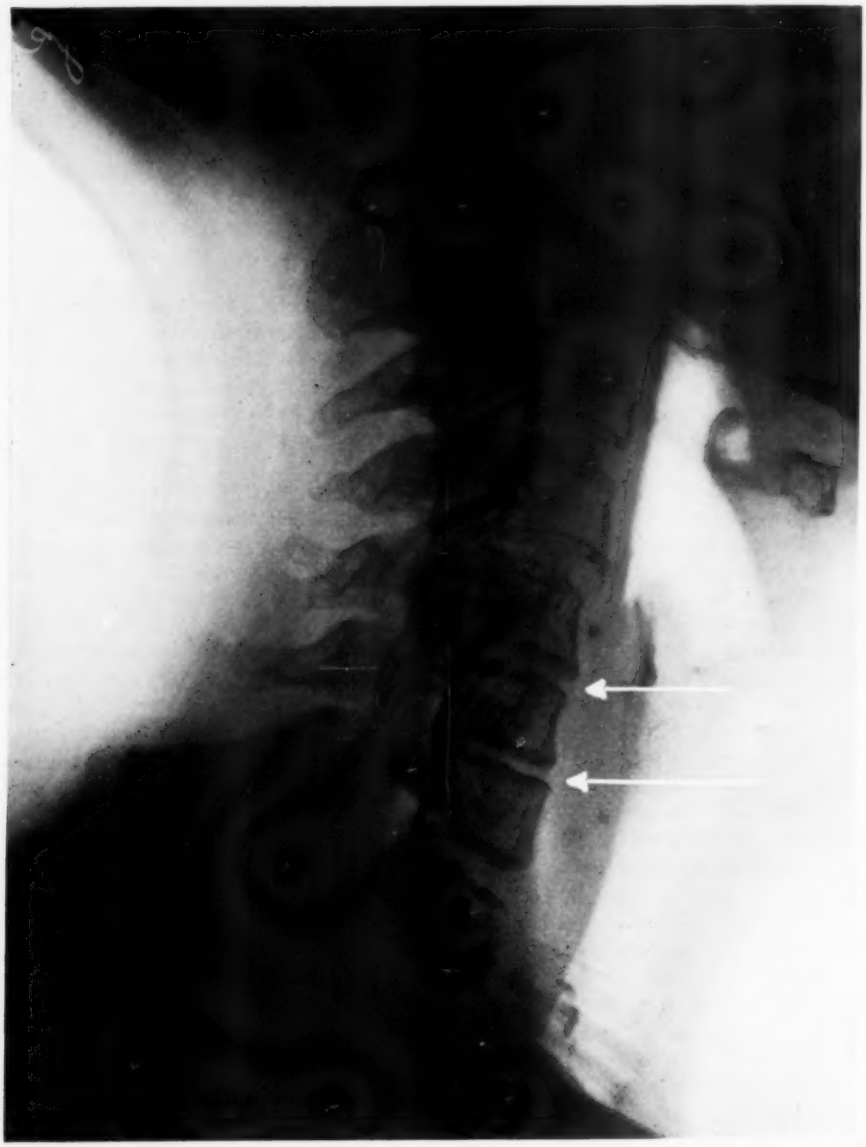

FIG. 1. *Case 1.* Showing narrowing of joint spaces between the fifth and sixth and sixth and seventh cervical vertebrae. Note the absence of lipping.

middle of her back over the sacrum and elevate the hand along the spine. This movement could be made passively although elevation of the hand along the vertebral column was more limited on the right side than it was on the left. The grip of the right hand was much weaker than that of the left. There was marked atrophy of

the soft tissues between the thumb and index finger of the right hand. No atrophy of the shoulder muscles on either side was present and the reflexes of both arms were present and normally active. There was no limitation of motion of the spine in the cervical region. The original diagnosis suggested on hearing her story and noting the atrophy of the small muscles of the right hand was an accessory cervical rib.

Roentgen findings revealed narrowing of the interspaces between the fifth and sixth and sixth and seventh cervical vertebrae. The bodies of the sixth and seventh vertebrae were flattened, their upper and lower surfaces irregular in contour and increased in bony density. There was moderate exostotic formation along the anterior borders of these vertebrae. There was no cervical rib. Roentgen diagnosis was atrophy of intervertebral discs with narrowing of the interspaces and hypertrophic spondylitis in the lower cervical spine. (Figure 2.)

This patient has obtained great relief from the pains in the shoulder and arm by forcible traction on the head. Relief was noticed following the first two treatments. All other methods of treatment were discontinued.

Case 3. V. K., a woman, 27 years of age. The chief complaint was pain in the lower part of the back of the neck between the shoulder blades and over the shoulders. (This was one of the two cases giving pain in the neck as the chief complaint.) She had experienced recurrent pain in the back, shoulders and lower neck for several years. She felt that her troubles began following a diving accident and later a fall from a horse. There has been no radiation of pain down the arms. She has found it difficult to turn the head to the left when the pain was present.

Physical examination revealed a healthy young woman with no limitation of movement in the shoulder joints on passive or active manipulation. There was a localized tender spot over the second dorsal vertebra and limitation of movements of the cervical spine. Turning the head to the extreme right or left was difficult and painful. Hyperextension of the neck as in lifting the head when the patient was in a prone position was also very painful.

Roentgen findings showed a deviation of the cervical axis due to anterior displacement of the third and fourth cervical vertebrae. No bony pathologic lesion was seen within the bodies of these vertebrae. The intervertebral space between the fifth and sixth cervical vertebrae was narrower than the other intervertebral spaces. There was no demonstrable abnormality in the thoracic spine. The roentgen diagnosis was: a definite abnormality in position of the cervical spine probably post traumatic with narrowing of one intervertebral space. (Figure 3.)

This patient was treated by traction on the head while lying in a supine position. The head was slowly turned from side to side while traction was exerted. Considerable relief was experienced following the first treatment. Physiotherapy in the form of traction and deep massage caudally over the upper thoracic spine while the patient was required to elevate the head and rotate it resulted in complete relief following three treatments.

Case 4. A. K. Z., a male banker, 53 years of age. The chief complaint was pain on raising the left shoulder, and a localized painful spot on the lower end of the right radius just above the wrist. The pain and limitation of movement in the left shoulder had gradually been increasing for the past several months. Discomfort was most marked during the night and early in the morning. It was difficult for him to raise the left arm when he put on his coat. Massage, heat, diathermy and baths had been used with no relief. He had also been informed that the pain in his shoulder was the result of an increase in the blood uric acid (diagnosed as a case of "uric acid diathesis") but he had obtained no relief from the use of atophan and other remedies. The left arm felt weak and heavy. For the past two weeks he had begun having a painful spot on the lower end of the right radius and felt that the

right hand was not as strong as formerly. His chief concern was a fear that he was developing a paralysis that would invalid him. One physician had frightened him badly by explaining that the pain in the left shoulder was the result of an aortitis.

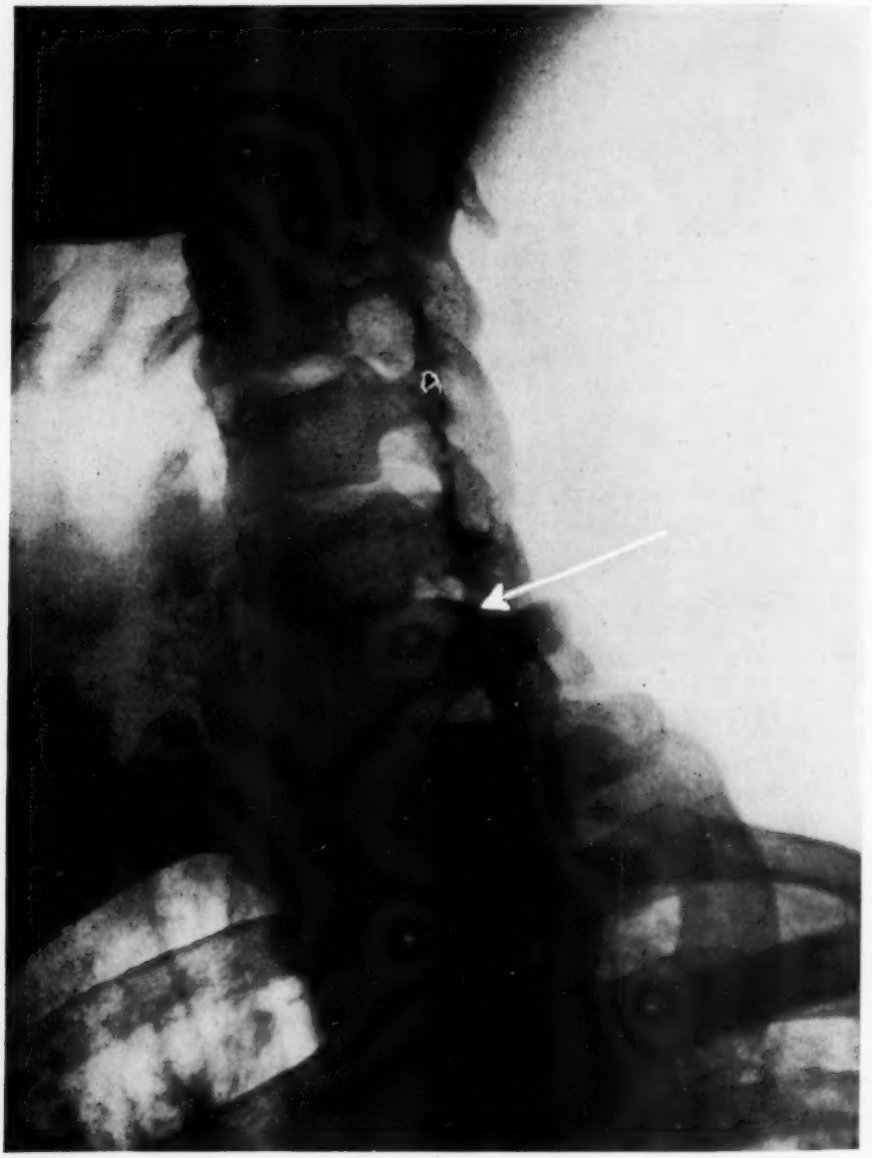

FIG. 2. *Case 2.* Oblique view showing actual narrowing of one of the intervertebral foramina.

Examination revealed a well nourished male who was not acutely ill. There was no limitation of neck movement in any direction. It was impossible for the patient to elevate the left arm above his head. He could not internally rotate this arm and place the left hand behind his back. On relaxation it was possible to move the left

shoulder joint freely by manipulation of the arm. There was no local tenderness over the painful spot over the lower end of the right radius. Careful physical examination did not reveal any evidence of aortitis. Blood pressure was normal and the

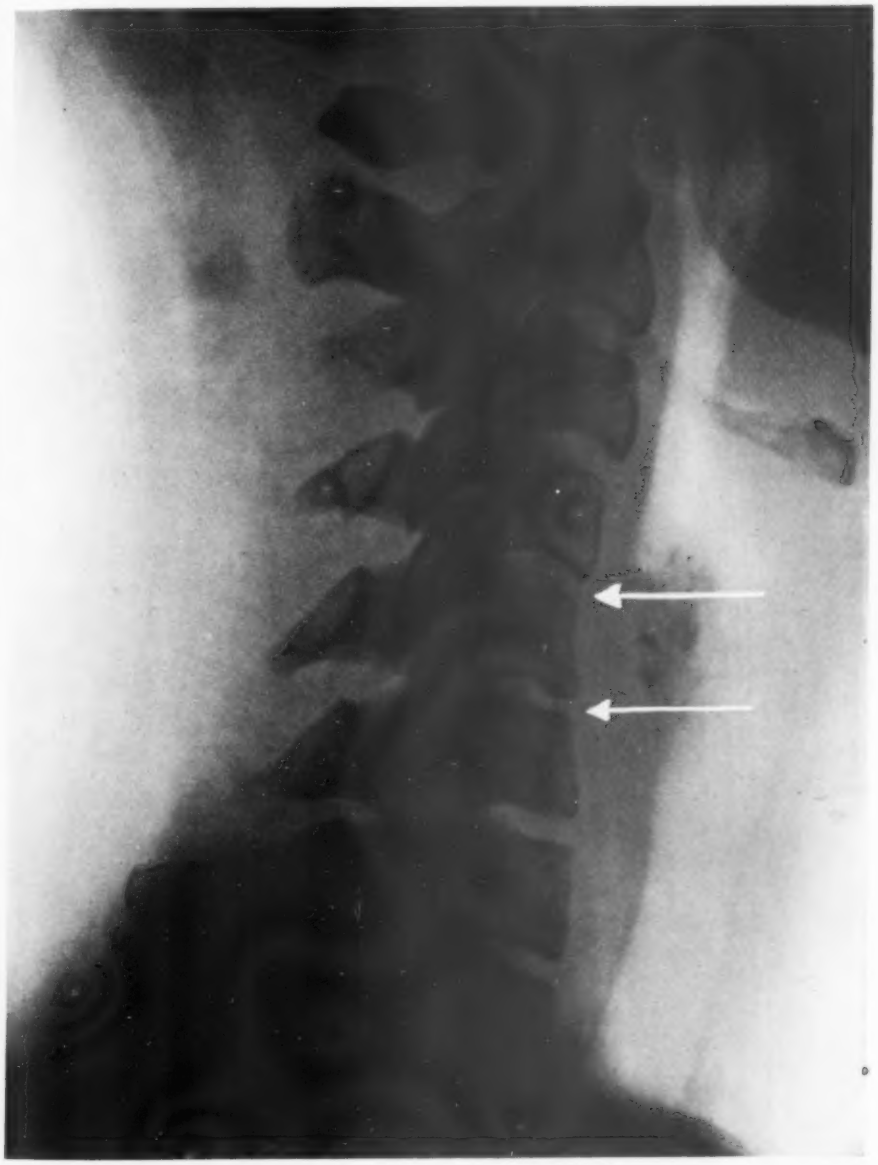

FIG. 3. *Case 3.* Showing deviation of the cervical axis due to anterior displacement of the third and fourth cervical vertebrae and narrowing of the interspace between the fifth and sixth cervical vertebrae.

cardiac contour was within normal boundaries. He was advised to have a roentgen-ray examination of the cervical spine and for the sake of reassurance to have also a roentgen-ray examination of the chest.

Roentgen findings revealed a classical hypertrophic spondylitis of the lower cervical spine with lipping present on the anterior lips of the fifth and seventh cervical vertebrae. There was also a marked narrowing of the interspace between the fifth and sixth and the seventh cervical and first thoracic vertebrae. (Figure 4.)

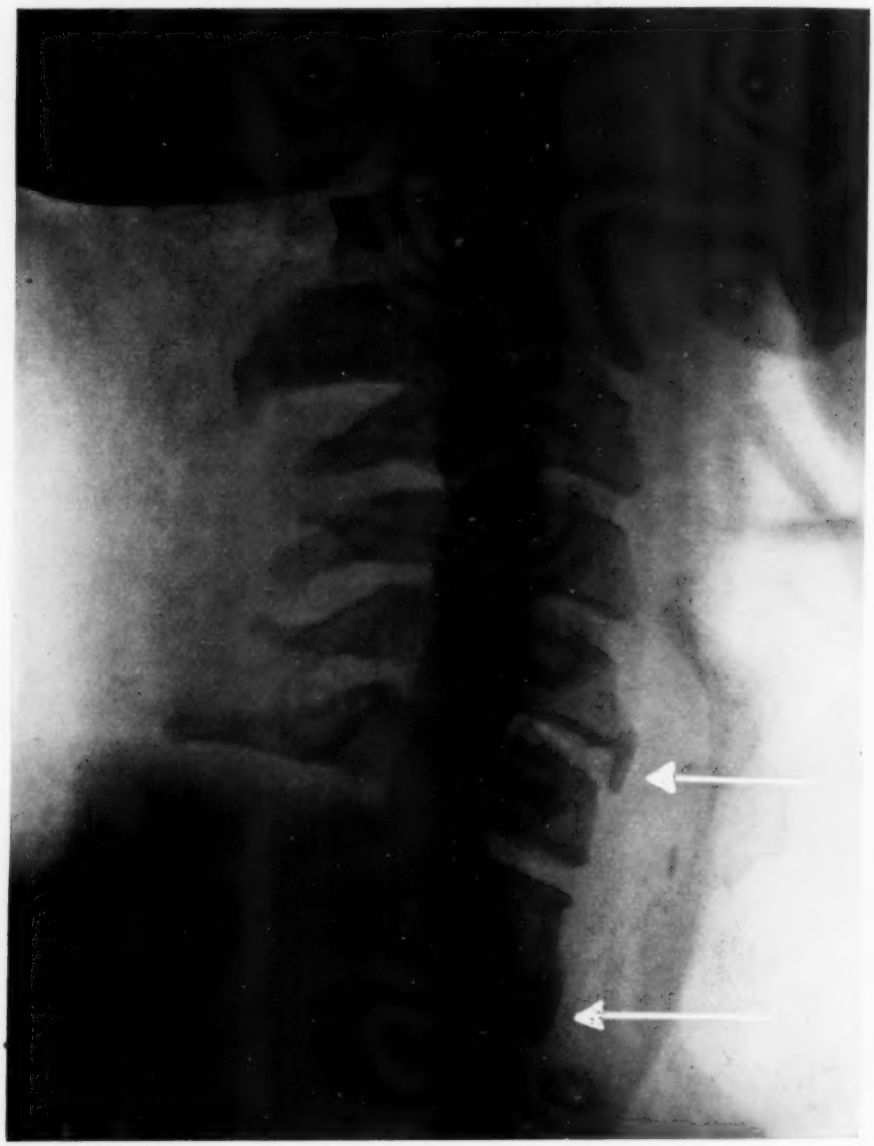

FIG. 4. *Case 4.* Showing hypertrophic spondylitis of the lower cervical spine with lipping of vertebral bodies and narrowing of the intervertebral spaces.

The patient was advised to have a series of deep roentgen-ray and short wave treatments over the cervical spine combined with traction treatments. Although the patient was a well educated, intelligent individual he proved to be a skeptic and sought further medical advice. About a week later the patient returned quite worried over

the fact that further study had revealed that his heart was responsible for the pain in the left shoulder while the pain in the right radius was the result of a fracture. The patient was naturally greatly upset. We again advised him that his cardiac findings were normal and that the changes in his cervical spine were quite sufficient, in our

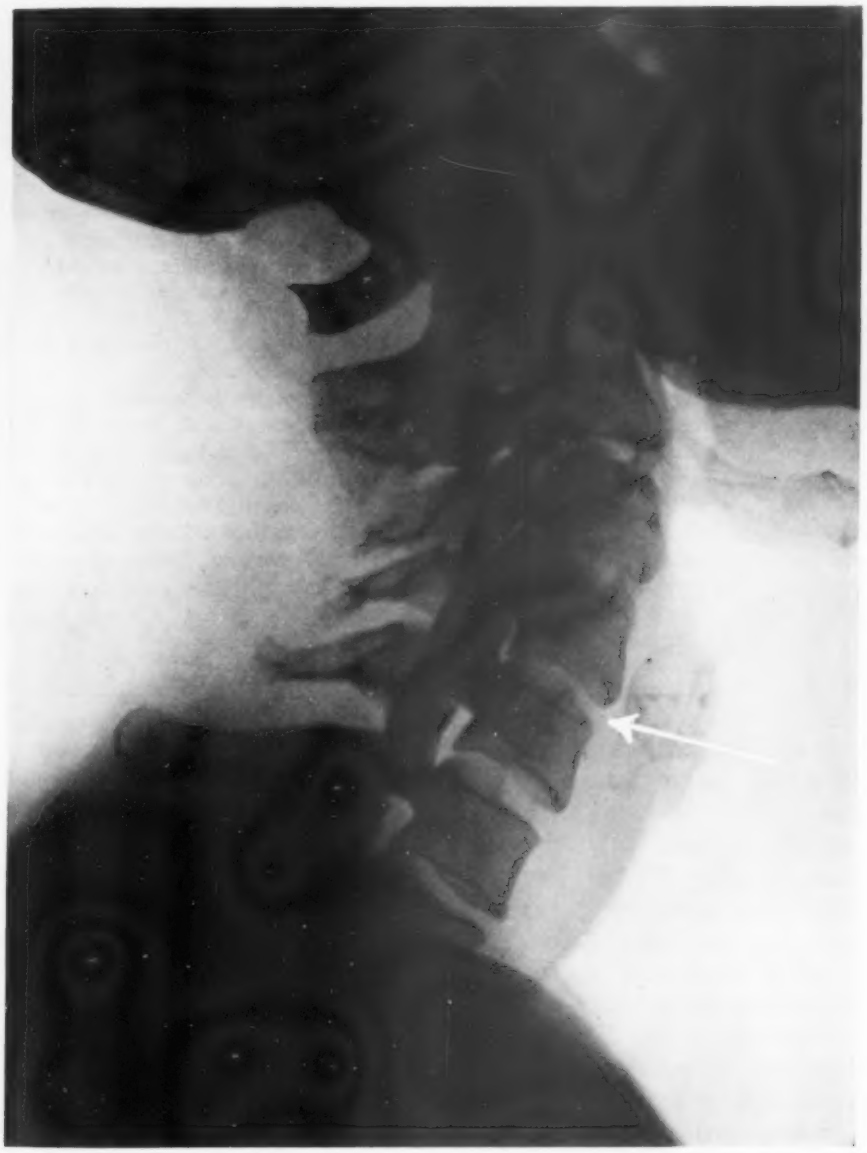

FIG. 5. *Case 5.* Showing narrowing of the interspace between the fourth and fifth cervical vertebrae with changes suggesting infectious arthritic involvement.

opinion, to be responsible for the symptoms in the left shoulder. He was advised that we could find no evidence of a fracture in the right radius and that in all probability the pain complained of in this region was also referred pain secondary to the narrowing of the interspace in the cervical spine. As he was still not fully con-

vinced roentgenograms of both wrists were taken to demonstrate the absence of any bony lesion in either radius. He then consented to undergo neck traction treatment. The local pain in the right wrist disappeared following the first three treatments and there was marked improvement of the symptoms in the left shoulder within a week. Treatment was continued for two weeks and up to the present time (one month) there has been no recurrence of pain in either upper extremity.

Case 5. M. F., a woman teacher, 27 years of age. This patient was first observed by one of us in September 1932 at which time she complained of pain in the right arm and shoulder of nine months' duration. This pain had gradually increased in severity and was variable in its intensity. Sometimes the pain was so severe that it made her cry from discomfort during the night. Movements of the right arm, especially such movements as were involved in combing her hair, were exceedingly uncomfortable. She had also noticed that writing, sewing or knitting was associated with a feeling of weakness and fatigue in the right arm and hand.

Examination revealed no actual involvement of the shoulder joint and movements were quite free in all directions. There was no muscular atrophy of the shoulder or arm. There was limitation of movement of the neck laterally with muscular spasm when extreme lateral movements were attempted. A local pain spot was present under the right scapula.

Roentgen findings revealed that the intervertebral space between the fourth and fifth cervical vertebrae contained a few hazy calcifications. The anterior ligament connecting the bodies of these two vertebrae was calcified and the whole interspace was narrowed. The upper thoracic spine was normal. The changes in the cervical spine had the appearance of those seen in the infectious rheumatic type of arthritis. (Figure 5.) Search for foci of infection was instituted and the teeth carefully cared for. The patient experienced some relief from autohemoclysis and sterile milk injections intramuscularly. Salicylates had more effect in this case than they did in most of the other cases of our series. Traction on the neck, which was prescribed first, gave in this instance only partial relief.

Discussion

In the five cases presented we have attempted to select histories demonstrating the different types of roentgen findings observed in our group of 50 cases. It will be noted that hypertrophic, post traumatic and rheumatoid changes have been included. Some of the patients showed no actual bone change of either the hypertrophic or rheumatoid type. All of the patients in this group had clear cut narrowing of one or more intervertebral spaces.

If one studies the relationships of the intervertebral foramina through which the nerves pass as they leave the spinal canal in the cervical region, it is quite obvious that narrowing of the interspaces between the vertebrae can and does change the diameter of these foramina. This narrowing can of course be doubly troublesome if there should happen to be exostosis formation around the foramen as well as atrophy of the intervertebral disc. Consideration of the relationships of these foramina also helps to explain why some patients have found it much more comfortable to sleep with the head propped forward since it will be seen that this position tends to widen the foramina while hyperextension increases symptoms because the borders of the foramina shorten the diameter in this position. Any inflammatory changes occurring around the nerves as they pass through these foramina

would also tend to aggravate the situation. Referred pain along the distribution of the fibers involved then takes place.

The middle and lower cervical regions were most commonly involved in our cases. This gives us a clue as the cause of the frequent shoulder pain. The fourth cervical segment supplies the sensory innervation over the top of the shoulder, and the fifth cervical segment supplies the sensory innervation of the outer surface of the arm between the shoulder and elbow. The deltoid muscle is supplied by nerve fibers derived from the fifth and sixth cervical segments. Shoulder pain and limitation of certain types of shoulder movement should be an indication for study of the cervical spine. This is especially true of pains that are not associated with actual arthritic changes in the shoulder. One of the most common mistakes in regard to these shoulder pains is to regard them as indicative of heart disease.

It was pointed out at the beginning of this paper that most of our patients were over 50 years of age. If there is any indication of precordial distress or if the pain is limited to the left shoulder and arm it is rather natural to check on the state of the heart and large blood vessels. It must be remembered that these elderly individuals usually have aortic shadows more dense than those seen in younger people and that the diagnosis of an aortitis or aortic sclerosis as the cause of the referred pain should be made with caution unless very obvious pathology exists. On the basis of our observations we strongly advise that patients with shoulder pains or precordial distress be subjected to a fluoroscopic examination of the cervical spine as well as roentgen examination of the heart and great blood vessels.

The problem as to the actual etiology of hypertrophic arthritis of the spine is still unsettled. The observations made in our series of cases may help to explain the formation of exostoses seen in this type of arthritis. Since all cases in this group have shown a consistent narrowing of one or more interspaces we are led to believe that this narrowing may be the first change of importance that takes place in many or perhaps all of these cases that later develop hypertrophic spondylitis. The thinning of the intervertebral disc must greatly increase the trauma of the vertebral bodies especially along their margins. This traumatic factor alone could in time be responsible for sufficient irritation along the vertebral margins to produce the formation of exostoses and the lipping so frequently seen in this disease. This is being offered merely as a possible explanation but corresponds to the dog experiments of Compere and Keyes.[9, 10]

We are inclined to agree with Hanflig in regard to his statement that these cases are quite common. If they are kept in mind and actually looked for they will be seen from time to time in every physician's office. They constitute a group that is commonly misdiagnosed repeatedly and that frequently becomes medical "drifters" because of the absence of physical findings in the neck. This can be largely avoided by more careful history taking and roentgenological examination. Furthermore the question of referred pain in relation to changes in the cervical spine should be constantly

kept in mind when dealing with problems involving pain or disturbed movement of the neck, upper extremity and chest. Close questioning of these patients will frequently reveal severe trauma of the spine at some previous time, often many years earlier.

Some of these patients obtain marked relief by means of neck traction. Hanflig's technic of traction using a Sayres sling suspension with block and tackle arrangement is perhaps the most simple method. Manual traction and manipulation will give satisfactory results in some cases although it is exceedingly strenuous exercise for the manipulator. Some cases are relieved greatly by the use of ultra short wave therapy directly over the cervical spine. The use of soft rubber soles and heels is advisable for all patients suffering from pathologic lesions in the cervical spine.

Further discussion of the roentgen findings observed in this group of cases is being presented in a subsequent communication.

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ACUTE PNEUMONITIS *

By William H. Allen, M.D., F.A.C.P., *Fort Sam Houston, Texas*

It is doubtful if there is anything in medicine presenting greater difficulty in classification than the so-called respiratory diseases. In every outbreak the problem arises when to cease the use of such terms as nasopharyngitis and acute bronchitis in order to adopt the equally indefinite one of influenza. One is confronted with the same difficulty in placing the pneumonias, though some progress is being made toward adoption of an etiological classification. It is with no wish to add to the prevailing confusion that we have found it useful to classify as acute pneumonitis a group of cases characterized by signs of respiratory infection, benign course, few physical signs, and roentgenographic evidence of a localized pulmonary involvement.

The dictionary gives pneumonitis as a synonym of broncho-pneumonia. Pathologically, this may be true but clinically and roentgenologically it represents a definite group, possibly a sub-group of the so-called broncho-pneumonias.

During the year 1935, there were admitted to the Medical Service of the Station Hospital, Fort Sam Houston, 2081 cases of respiratory disease. Of these, 53 were classed as primary lobar pneumonia, 16 as primary broncho-pneumonia, and 68 as acute pneumonitis. From the last I have selected 50 cases for analysis. It is doubtful whether this represents the true incidence of the condition as only in the more severe cases of respiratory infection were chest films made. As the diagnosis must be made almost solely by this means there appears to be no doubt that pneumonitis is generally overlooked. This is borne out by the paucity of reference to it in the literature.

Etiology. This is uncertain but as all these cases occurred in the general group of acute respiratory infections it may be assumed that a filtrable virus with a secondary invasion by the ordinary bronchial tract organisms was the causative factor. While pneumococcus typing is carried out in all primary pneumonias, no effort was made to do so in the majority of these cases here reported. In a few, group IV pneumococci were isolated; in others, no pneumococci were found.

Due to the regulations governing admissions to our service, the great majority of the patients reported were young, adult males, but one female being included in the present analysis. The minimum age was 9 and the maximum 51 with an average of 25.5. We are unable to judge of the true age and sex incidence of this condition.

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From the Medical Service, Station Hospital, Fort Sam Houston, Texas.

Pathology. As there were no deaths in this series or in others that I have seen no definite knowledge of the pathology exists. The lung lesion may be visualized as an inflammatory and exudative process extending from the bronchioles into the alveoli over a localized portion of a lobe or lobes. The involvement was predominantly of one or both lower lobes in 92 per cent

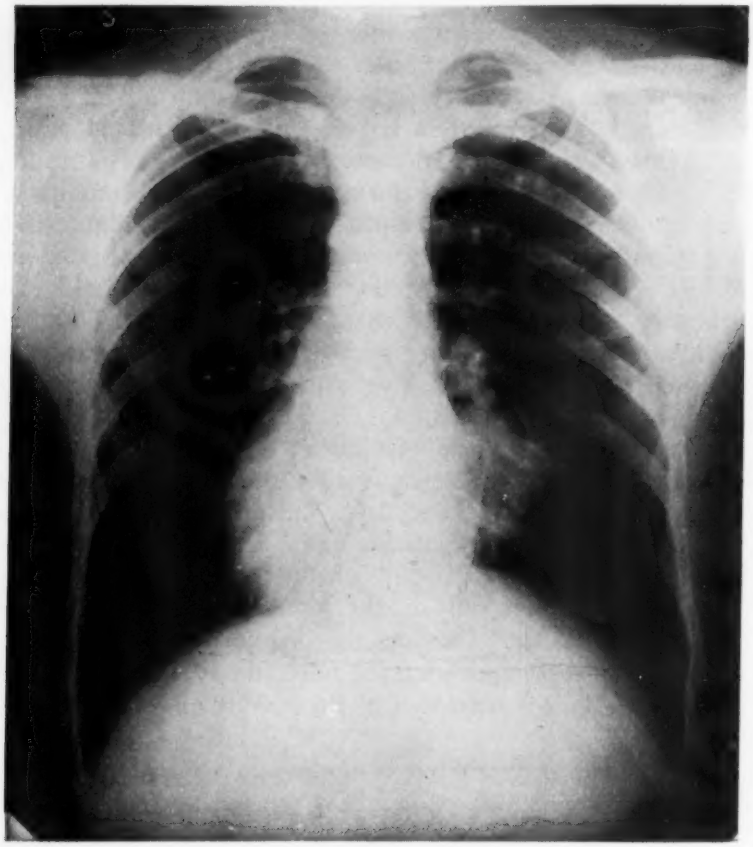

FIG. 1. Pneumonitis extending from the right hilum.

TABLE I

Lobes Involved

	Cases	Per cent
Right lower	18	36.0
Both lower	15	30.0
Left lower	11	22.0
Right all	2	4.0
Right middle	1	2.0
Right upper	1	2.0
Left upper	1	2.0
Both upper	1	2.0
	50	100.0

of our cases with the greater incidence on the right side. Taking the lungs as a whole, the right was involved in 44, the left in 24, and both in 32 per cent.

Symptoms. On admission the patients complained of the usual symptoms of acute respiratory infection—cough, fever, malaise, and "cold in the head." There was a noticeable absence of the ordinary symptoms of pneumococcus pneumonia, such as initial chill, sharp pain, and rusty sputum.

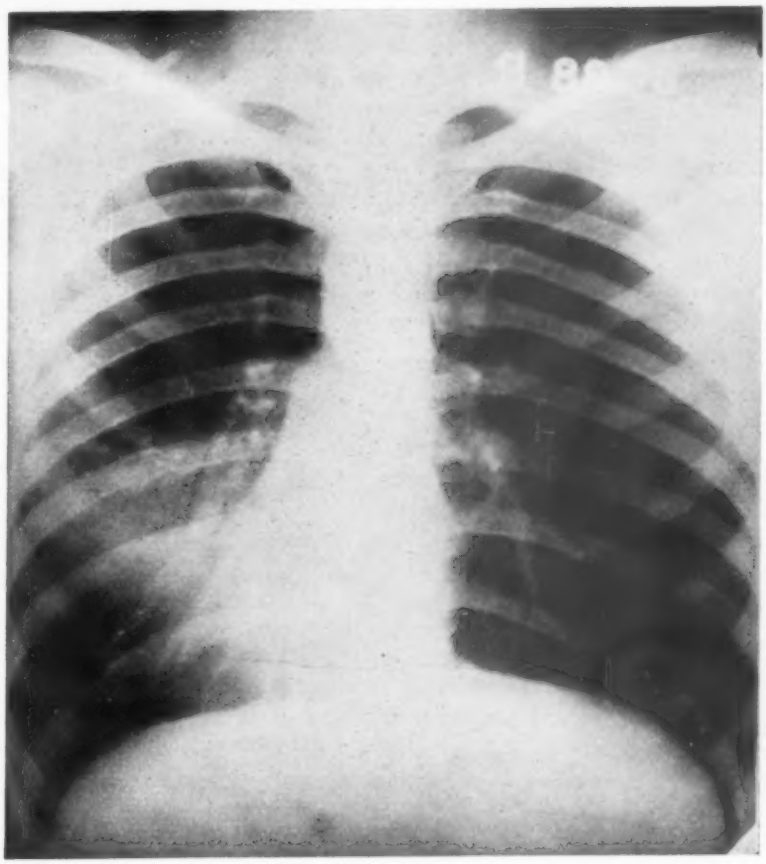

FIG. 2. Pneumonitis of left lower lobe.

When there was complaint of pain in the chest it was described as a dull aching or sense of fulness. In no case was there the stabbing pain of pleural involvement. This may be explained by the fact that the involvement was almost invariably central.

The maximum temperature was usually recorded within a day or two of the onset. Defervescence was commonly rapid though in a number of cases a low grade, irregular fever persisted for many days. The maximum temperature is shown in table 3.

TABLE II

Symptoms on Admission

	Cases	Per cent
Cough	43	86.0
Fever	35	70.0
Malaise	27	54.0
"Cold"	27	54.0
Pain or soreness in chest	15	30.0
Sore throat	14	28.0
Headache	14	28.0
Weakness	4	8.0
Chill	4	8.0
Nausea or vomiting	3	6.0
Bloody or blood-tinged sputum	2	4.0
Abdominal pain	2	4.0
Stiff neck	1	2.0
Vertigo	1	2.0
Night sweats	1	2.0

TABLE III

Maximum Temperature

	Cases	Per cent
99′–100′	4	8.0
100′–101′	9	18.0
101′–102′	10	20.0
102′–103′	15	30.0
103′–104′	7	14.0
104′–105′	5	10.0
	50	100.0

Physical Signs. These were conspicuous by their absence. As shown in table 4, 36 (72 per cent) had fine or medium moist râles over the involved area, while 10 (20 per cent) had no demonstrable signs. In a large proportion no râles were found at the time of admission, these appearing from one to three days later. Impaired resonance was found in but 3 (6 per cent) and broncho-vesicular breathing in but 1 (2 per cent).

TABLE IV

Physical Signs

	Cases	Per cent
Fine or medium râles	36	72.0
Coarse râles	3	6.0
Impaired resonance	3	6.0
Broncho-vesicular breathing	1	2.0
Friction rub	1	2.0
No signs	10	20.0

The maximum leukocyte count was below 14,000 in 78 per cent of the cases, and in 54 per cent it was 10,000 or less.

TABLE V

Maximum Leukocyte Count

	Cases	Per cent
5000– 7000	12	24.0
8000–10000	15	30.0
11000–13000	12	24.0
14000–16000	7	14.0
17000–20000	3	6.0
Above 20000	1	2.0
	50	100.0

Roentgenological Signs. Major Bowen of the Army Medical Corps, to whom I am indebted for the roentgenologic studies in these cases, has recently described the findings in influenzal pneumonitis as follows:

> Influenzal pneumonitis involves only a portion of a lobe, usually basal, though it has been seen in the upper lobes and involving more than one lobe without increase in symptoms. It extends outward from the hilus well into the parenchyma, occasionally reaching the periphery. The roentgen appearance is that of a confluent mottled fan or rounded area, usually of homogenous moderate density in the central portion, with the borders fading into the normal lung. It has the appearance of an exudative alveolar infiltration and is usually more localized and of more even density than the bronchopneumonias of childhood or than those which complicate adult diseases. The usual picture of broncho-pneumonia is a scattered mottling not confined to one lobe or sharply localized.[1]

In the present series, 44 per cent showed a single area of pneumonitis while 36 per cent had more scattered infiltration. Eighteen per cent had two areas of increased density, usually involving both lower lobes.

TABLE VI
Roentgenologic Signs

	Cases	Per cent
Single area of pneumonitis	22	44.0
Two areas of pneumonitis	9	18.0
Scattered infiltration	18	36.0
No definite signs	1	2.0
	50	100.0

Complications. These were rare. Three cases (6 per cent) developed acute maxillary sinusitis and one each, acute otitis media and urticaria. One case had a peritonsillar abscess with subsequent necrosis of the cervical lymph nodes, requiring operative intervention.

Prognosis. There were no deaths in this series. The maximum period of hospitalization was 91 days for the case with peritonsillar abscess and necrosis of the cervical glands, the minimum was nine days, and the average 28 days. This average is in excess of what might be expected in a civil hospital due to the fact that a soldier is not discharged until he is able to return to full duty but it serves to indicate what may be considered the length of convalescence. In the majority of cases hospitalization was prolonged by weakness and the persistence of cough and râles after all other symptoms and signs had subsided.

A better idea of the duration of the disease may be gained from the days of fever as shown in table 7.

TABLE VII
Duration of Fever

Days	Cases	Per cent
1–2	4	8.0
3–5	15	30.0
6–8	12	24.0
9–11	7	14.0
12–15	4	8.0
16–20	2	4.0
Over 20	6	12.0
	50	100.0

Treatment. This has been purely symptomatic. Emphasis has been placed on adequate nursing, free use of fluids, and a relatively high carbohydrate intake. Codeine has been used freely for the control of cough.

Summary

1. Acute pneumonitis is used as the designation for a form of respiratory infection characterized by a benign course, few physical signs, and roentgenologic evidence of a localized inflammatory process in the lung.

2. In the absence of deaths the pathology is unknown but it is assumed to be an extension of an inflammatory process from the bronchioles to the alveoli with exudation.

3. The symptoms are those of a moderate to severe respiratory infection.

4. The diagnosis must be made by roentgenography.

Reference

1. Bowen, A.: Acute influenzal pneumonitis, Am. Jr. Roent. and Radium Therap., 1935, xxxiv, 168–174.

DIVERTICULA OF THE STOMACH*

By Lay Martin, M.D., F.A.C.P., *Baltimore, Maryland*

Diverticula of the stomach are rarities. The average physician has had no experience with this abnormality, and this lack of experience is not limited to the clinical side of medicine; it is also found among the pathologists.

My interest in the subject was awakened by discovering a diverticulum of the stomach in a patient—a patient who wanted to know all about the condition: What should be the treatment—medical, surgical or none? What were the symptoms caused by the abnormality? Did it increase or decrease in size? What was the danger of perforation? How often should a re-examination be made? How often did it occur? What was the chance of malignant degeneration? As a result a study was made of the condition.

An exhaustive search through the archives of the History Department of the Johns Hopkins Hospital was unfruitful in revealing a single case diagnosed ante mortem. Not one was reported after laparotomy. Apparently none was reported by the roentgenologic department. The search was continued through the records of the pathology department and five cases were found. These and one living case are reported below.

Case Reports

Case 1. A physician, aged 40 years, consulted me complaining of indigestion, bloating, distention and at times a gnawing sensation which was partially relieved by food. He was concerned about himself to the point of believing that he had a duodenal ulcer. Certain factors, to him of serious import, had come into his life and made him quite tense. His story was typically one of anxiety neurosis. On physical examination nothing remarkable was noted.

Fluoroscopic examination of his stomach showed an unusual condition. Barium flowed freely through the esophagus and the cardiac orifice. The stomach was in good position, the rugae well defined and regular, and the tonicity normal. To the mesial side of the lesser curvature, in the upper fundo-cardiac portion, was a spherical mass, which was mobile, not tender, clearly defined, of smooth regular outline. This was connected to the stomach by a narrow pedicle; films, made later by Dr. J. W. Pierson, convincingly demonstrated its patency and that it connected the barium filled sphere with the stomach. Hours after the stomach was freed of barium, the diverticulum remained visible. The patient finally solved his personal problems and the gastric symptoms abated. The diverticulum is still as noted above.

Since 1920, five cases of diverticulum of the stomach have been noted in the department of pathology of the Johns Hopkins Hospital. They are given seriatem below. In none of these cases does the clinical history give

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From the Gastro-Intestinal Division of the Department of Medicine, Johns Hopkins Hospital and University.

any suggestion of the presence of the diverticulum and such symptoms as were manifest were located in other systems than the gastrointestinal.

Case 2. A 39-year-old negro female.

Anatomical diagnosis: History of sudden convulsive death at operation under procaine anesthesia. Operative wound in left thorax, cardiac hypertrophy, ascites,

FIG. 1. Showing diverticulum of the stomach soon after ingestion of barium sulphate.

bilateral hydrothorax, edema of back, chronic passive congestion of lungs, liver and kidneys. Diverticulum of stomach. Mitral insufficiency.

Macroscopic description: The stomach is normal in size and contains a small

amount of semifluid food. The mucosa shows postmortem digestion. At the dome of the cardia, there is a small diverticulum about 3 cm. across and bulging out about 2 cm. The musculature over this area is greatly thinned out and leaves practically nothing but the mucosa and serosa.

Microscopic description: All muscular coats except that of the mucosa disappear over a small area.

FIG. 2. Showing diverticulum of stomach six hours after ingestion of barium sulphate.

Case 3. A 59-year-old white male.

Anatomical diagnosis: Acute and chronic verrucose endocarditis of aortic and mitral valves. Aortic stenosis and insufficiency, slight scarring of myocardium,

cardiac hypertrophy, chronic passive congestion of lungs and viscera, clubbing of fingers, edema of ankles, mural thrombosis, pulmonary emboli, infarcts, and edema. Generalized arteriosclerosis, old scars in kidneys, prostatic hypertrophy, slight hypertrophy of bladder muscle. Dental caries. Diverticulum of stomach. Papillary cystadenoma of kidney. Thrombi in prostatic plexus.

Macroscopic description: Near the cardiac orifice the stomach wall is thinned out over an area of about 2 cm. in diameter so that a little pouch is formed.

Microscopic description: Sections of the stomach taken through the pouch show normal serosa and mucous membrane. The muscular layer is scant.

Case 4. A 60-year-old white male.

Anatomical diagnosis: Hypophyseal tumor pressing on optic chiasm with atrophy of right optic tract and nerve. Calcified area on surface of right upper lobe with fibrous pleural adhesions. Caseous tuberculous lymph nodes along trachea and hilum of right lung. Disseminated tubercles in liver, lungs, spleen, kidneys. Obesity. Diverticula in pylorus.

Macroscopic description: Just proximal to the pyloric valve there are two diverticula measuring 1 cm. in diameter and 1 cm. deep, over which the mucosa appears to be intact. Dr. MacCallum: "At the pylorus there is a sacculation with complete lining of mucosa."

Microscopic description: The walls of the one diverticulum seen are normal.

Case 5. A 16-year-old negro female.

Anatomical diagnosis: Acute necrosis of liver, small liver, jaundice, hemorrhages into endocardium, puerperal uterus, diverticulum in pyloric position of stomach, accessory pancreas. Fresh ulcer in duodenum, diffuse enlargement of thyroid. Calcified vessels in corpus striatum.

Macroscopic description: Stomach—about 1 cm. from the pylorus there is a small diverticulum in the stomach wall with an opening measuring 5 mm. in diameter. It is about 1 cm. deep and there seems to be a palpable little tumor at the end of the diverticulum. The lining of the little cavity seems to be normal pale mucosa. There is also a duodenal ulcer.

Microscopic description: Stomach: There are two sections which show the stomach. The opening of the small diverticulum is missed. The section one was cut further to show it if possible. However, one shows the space in the wall of the stomach and at the base the little nodule which turns out to be for the greater part made up of gland tissue. There are a few areas of pancreatic tissue.

Case 6. A 28-year-old negro female.

Anatomical diagnosis: Encapsulated caseous tubercles in lungs, hyaline and caseous tubercles in tracheal lymph nodes. Disseminated tubercles in spleen, liver, kidneys, intestines and lung. Tuberculous meningitis. Infarcts in spleen, purulent tonsillitis, lobular pneumonia. Cyst in left ovary with hemorrhage. Scarring of pancreas. Syphilis (positive Wassermann). Diverticula of stomach.

Macroscopic description: The fundus of the stomach is thinned out, and on the ventral surface of the greater curvature, near the cardiac end, four shallow excavations are seen. Peculiar punctate excavations measuring less than a millimeter, are generously scattered in the mucosa near the cardiac end of the greater curvature, more posterior than the larger ulcers. There is a diverticulum lined with normal stomach mucosa near the pyloric end of the fundus.

Microscopic description: The mucosa, muscularis, muscular layer and serosa are intact.

Discussion

The subject about to be discussed offers one of the best examples of that common fault of the medical historian, i.e. the acceptance of previous au-

thors' interpretations of the writings of others. The writers who have made any attempt to outline the history of our knowledge of gastric diverticula all refer to Helmont as being the first to see and report the finding. Voigtel is the authority generally cited for first mentioning Helmont. Those who do not mention Voigtel assert that Helmont in 1804 reported the first case.

To explain the continued reiteration of this inaccuracy, we may best start with the report by M. Fournier [3] in 1774. He performed an autopsy on a former patient, whose clinical course had been completely mystifying to him. His description of what he observed on section is of no immediate interest to us until he says that the stomach was filled with numerous foreign bodies such as pieces of iron, wood, etc., and he writes: "La forme de l'estomac était un quarrè long. On y distinguait aisément quatre faces chacune de quatre pouçes de largeur. L'ayant ouvert nous y trouvâmes toutes les piece détaillés ci-après dans le rapport et tellement arrangées que l'on aurait dit qu'une main adroite les eut placées chacune de façon qu'elles eussent occupées le moins de place possibles." At no point in his article is there any reference to a sac or a diverticulum. In 1804 Voigtel [4] referred to Fournier's patient, and commented upon the numerous articles swallowed by him. In describing the pathological findings (on page 512) he says: "Im Schlunde fand man ein grosses Stuck Holz in Magen aber, innerhalb einen besondern Sack." Surely a misrepresentation of the facts as reported by Fournier.

Another factor which has apparently helped confuse the unwary was Voigtel's [4] description of a duodenal diverticulum on page 504, under the general subject of Hydropis Ventriculi. He writes: "In der mitte des Pförtners hing ein mit Wasser gefüllten Sack, der eines Fingers lang und einen Zoll dick war, und sich in der Zwölffingerdarm erstreckte." Citing previous references to the subject he refers to page 154 of Moebius' [2] book, which was published in 1661. Here the author may be quoted: "Hydropis Ventriculi meninit Lazarus Riverus in observat communie p. 364 in quo tantus tumor ejus ut ex aperto nonanginta librae aguae effluerent."

It so happens that on page 137 of this same volume of Moebius there is a reference to Helmont: "sacculum ventriculi annatum et lapidilus refertum conspexit Helmont." Not only does Voigtel not refer to Helmont but his reference to Fournier is incorrect, besides that the diverticulum he himself observed and described was connected with the duodenum.

Another mistake which has been carried on down in the literature is in regard to a gastric diverticulum alleged to have been described by Vasquez [5] in 1859. A soldier died some time after being badly jarred. On section there was revealed: "existencia sobre su parte superior y lado derecho de enorme saco, ciego, al porecer, mas en comunicacion con el esófacgo por pequenos aquejeros que a modo de regadera daban paso a las líquidas bebidos de que estaba llena su cavidad, y cuyas paredas de mas de un pulgada de grosor ostentaban en su superficie esterna diversas máticos desde el violado

TABLE I

Reference	Author	Age	Sex	Position	Walls of Sac	Observation	Year Reported	Symptoms	Remarks
1	Baillie			not stated	thinned	autopsy	1793	not stated	coins found in pouch
11	Thorel			cardiac	thin muscle mucosa and serosa	autopsy	1895	not stated	
12	Kleine	45	Male	lesser curvature prepyloric	mucosa and thick muscle	operation	1895	not stated	
				lesser curvature prepyloric	muscle—no mucosa	autopsy	1895	not stated	
				Prepyloric	thin muscle, mucosa and serosa	autopsy	1895	not stated	
13	Kolaczek	45	Female	lesser curvature mid portion	intact	operation	1895	pseudo ulcerous	cured
14	Grassberger	73	Male	posterior wall near pylorus	muscle thin, mucosa and serosa intact	autopsy	1897	pseudo ulcerous	
15	Schulten	25	Female	lesser curvature	intact	autopsy	1897	not stated	
16	Ferguson	34	Female	near cardiac orifice	mucosa and serosa	autopsy	1898	not stated	
17	Zahn	53	Male	near cardiac orifice	muscle thin, mucosa and serosa intact	autopsy	1899	not stated	
18	Hamilton	59	Male	near cardiac orifice	not stated	autopsy	1901	not stated	
20	Hirsch	46	Male	near cardiac orifice	mucosa and serosa intact	autopsy	1903	not stated	
22	Küss	61	Male	greater curvature prepyloric	thin muscle, mucosa intact	autopsy	1905		
27	Jones	33	Male	anterior wall near pylorus	mucosa and serosa only	operation	1909	yes	cured
29	Broman	Embryo		not stated	intact	autopsy	1910		
28	Keith	70	Female	near cardiac orifice	muscle thin, mucosa and serosa intact	autopsy	1910		museum specimen
		adult		near cardiac orifice	mucosa and serosa only	autopsy	1910		museum specimen
30	Handtmann	35	Male	near cardiac orifice	walls intact and filled with blood	autopsy	1912	none	
33	Boreszeky	53	Male	greater curvature near pylorus	intact	operation	1914	pseudo ulcerous	cured
		32	Male	lesser curvature near pylorus	intact	operation	1914	pseudo ulcerous	cured
35	Brown	29	Female	lesser curvature near pylorus	intact	operation	1916	yes	cured
36	Secher	31	Male	near cardiac orifice	muscle thin, mucosa and serosa intact	autopsy	1917	not stated	
40	Mellon, et al.	54	Male	greater curvature mid portion	walls intact	x-ray and operation	1921	yes	cured
41	Oberling	42	Female	lesser curvature pyloric	mucosa and serosa only	x-ray and autopsy	1923	yes	died
42	Akerlund	29	Female	near cardiac orifice		x-ray	1923		also duodenal ulcer
		53	Female	near cardiac orifice		x-ray	1923		
		40	Female	near cardiac orifice		x-ray	1923		also diverticulum of duodenum
		42	Female	near cardiac orifice		x-ray	1923		
43	Rothbart	63	Female	near cardiac orifice		x-ray	1923		
		38	Female	lesser curvature mid portion		x-ray	1923		
44	Tupper	43	Male	lesser curvature near pylorus	muscle thin, mucosa and serosa intact	x-ray and operation	1923	present	cured

TABLE I—*Continued*

TABLE I—*Continued*

Reference	Author	Age	Sex	Position	Walls of Sac	Observation	Year Reported	Symptoms	Remarks
45	Ravenel	65	Female	near cardiac orifice two sacs		x-ray	1923	yes	
46	Coleschi		Male	greater curvature mid portion		x-ray	1923	pain	
48	Stolz and Hickel	48	Female	greater curvature pyloric	intact	x-ray and operation	1923	present	cured
50	Fleischner	62	Male	near cardiac orifice	mucosa and serosa only	autopsy	1924	complication	abdominal cancer
		72	Female	near cardiac orifice	muscle thin, mucosa and serosa intact	autopsy	1924	complication	abdominal cancer
51	Emery	adult	Female	near cardiac orifice		x-ray	1924	questionable	
		48	Male	near cardiac orifice		x-ray	1924	questionable	
52	Perusia	adult	Male	lesser curvature mid portion		x-ray	1924	present	
55	Delherm et al.		Female	lesser curvature mid portion	no note	x-ray and operation	1925	present	cured
56	Southerland	51	Male	greater curvature and pylorus, two pouches	not stated	x-ray and operation	1925	bleeding	cured
57	Weiss	49	Male	lesser curvature near pylorus	intact	x-ray and operation	1925	pseudo ulcerous	cured
58	Gray	32	Male	near cardiac orifice		x-ray	1925	none	
54	Hurst and Briggs	35	Female	near cardiac orifice		x-ray	1925	yes	postural drainage
		58	Female	near cardiac orifice		x-ray	1925	yes	postural drainage
60	Bordoni	39	Female	near cardiac orifice		x-ray	1926	yes	
61	Thomson	45	Male	near cardiac opening	muscles thin, mucosa thin	x-ray and operation	1926	yes	questionable
62	Brandt	64	Female	near cardiac orifice	intact	autopsy	1926	no	
63	Lawson	50	Female	near cardiac orifice		x-ray and operation	1926	no	not found at operation
64	Jonas	42	Male	lesser curvature mid portion		x-ray	1926	yes	
65	Pearlstein	43	Female	near cardiac orifice		x-ray	1926	yes	
68	Bernstein	34	Female	near cardiac orifice		x-ray	1928	none	
69	Kalbfleisch	39	Female	near cardiac orifice		x-ray	1928	none	
70	Goodwin	33	Female	near cardiac orifice		x-ray	1928	yes	
71	Pernkopf	Embryo		near cardiac orifice	intact	autopsy	1928		
72	Pansdorf	48	Female	lesser curvature near pylorus	intact	x-ray and operation	1929		
73	Sinclair	Infant		not stated	intact	operation	1929	yes	cured
75	Liljedahl	25	Female	near cardiac orifice		x-ray	1929	none	
76	Allan	43	Female	near cardiac orifice	muscle thin, mucosa intact	autopsy	1930	none	
77	Geyman	63	Male	near cardiac orifice		x-ray	1930	yes	
		34	Female	near cardiac orifice		x-ray	1930	yes	
78	Santoro	18	Female	near cardiac orifice		x-ray	1930	questionable	
79	Ottonello	65	Female	near cardiac orifice		x-ray	1930	questionable	
		12	Male	near cardiac orifice		x-ray	1930	questionable	
80	Beutel and Mahler	69	Male	lesser curvature mid portion		x-ray and gastroscope	1930	yes	
81	Anziolotti	59	Female	greater curvature mid portion		x-ray	1930	yes	

TABLE I—*Continued*

Reference	Author	Age	Sex	Position	Walls of Sac	Observation	Year Reported	Symptoms	Remarks
82	Lenarduzzi	48	Female	greater curvature mid portion		x-ray and operation	1931	pain	not found at operation
		54	Female	lesser curvature mid portion		x-ray	1931	questionable	2 small diverticula
		16	Female	near cardiac orifice		x-ray	1931	questionable	also diverticulum of colon
85	Laurell	18	Female	greater curvature upper portion		x-ray	1931	none	
83	Gile	7	Female	lesser curvature near pylorus	intact	x-ray and operation	1931	yes	cured
84	Pendergrass			near cardiac orifice		x-ray	1931	not stated	
87	Bell and Golden	49	Female	near cardiac orifice		x-ray	1932	questionable	
		37	Female	near cardiac orifice		x-ray	1932	yes	not found at operation
		30	Female	near cardiac orifice		x-ray	1932	yes	
		45	Male	lesser curvature mid portion		x-ray	1932	questionable	associated duodenal ulcer
88	Barsony and Koppenstein	65	Male	lesser curvature mid portion		x-ray	1932	questionable	associated duodenal ulcer
		54	Male	near cardiac orifice		x-ray	1932	no	
		20	Male	near cardiac orifice		x-ray	1932	yes	
		63	Male	near cardiac orifice		x-ray	1932	yes	helped by atropine
		12	Female	near cardiac orifice		x-ray	1932	no	
		50	Male	near cardiac orifice		x-ray	1932	no	
89	Gutzeit and Kuhlmann	56	Male	near cardiac orifice		x-ray and gastroscope	1933	questionable	
		29	Male	near cardiac orifice		x-ray and gastroscope	1933	no	
90	Bonnet	44	Male	near cardiac orifice	muscle thin, mucosa and serosa intact	x-ray and operation	1934	bleeding	cured
91	Rivers et al.	36	Male	near cardiac orifice	all coats thinned	x-ray and operation	1935	present	cured, ulcer at pylorus
		28	Female	near cardiac orifice	all coats thinned	x-ray and operation	1935	present	no note
		43	Male	greater curvature mid portion	all coats thinned	x-ray and operation	1935	present	no note
		30	Female	prepyloric	all coats thinned	operation	1935	present	no note
		26	Female	prepyloric	all coats thinned	operation	1935	present	cured
		51	Male	prepyloric	all coats thinned	operation	1935	present	blood in diverticulum
		49	Male	prepyloric	all coats thinned	operation	1935	questionable	ulcer also present, cured
		59	Female	prepyloric	all coats thinned	operation	1935	present	not cured, also had duodenal ulcer
		56	Female	cardiac	all coats thinned	autopsy	1935	no note	
		49	Male	cardiac	all coats thinned	autopsy	1935	no note	
		44	Female	cardiac	all coats thinned	autopsy	1935	no note	
		55	Female	cardiac	all coats thinned	autopsy	1935	no note	
92	Freiliche et al.	24	Female	cardiac		x-ray	1935	present	
	Martin	44	Male	lesser curvature mid portion		x-ray	1935	none	
		39	Female	cardiac	mucosa and serosa only	autopsy	1935	none	
		59	Male	cardiac	intact muscle thin	autopsy	1935	none	
		60	Male	lesser curvature prepyloric	intact	autopsy	1935	none	
		28	Female	lesser curvature prepyloric	intact	autopsy	1935	none	

al claro, propio de las membranas." In this instance there was a traumatic diverticulum of the esophagus, not of the stomach.

In spite of the rarity of the abnormality there is quite an amount of literature on the subject, and to avoid the possible continuation of the errors noted above the information presented below has been taken from the original reports. The compiled data on the 103 uncomplicated pulsion diverticula are presented in table 1, and the cases are arranged in their order of publication. Besides this number, the other 22 more or less complicated cases are reported in their turn.

Reports are available from many countries. The earliest authentic case I have found is that of Thomas Baillie,[1] who writes: "A part of the stomach is occasionally formed into a pouch by mechanical means, although very rarely. I have seen one instance of a pouch being so formed, in which five halfpence had been lodged. The coats of the stomach were thinner at that part, but were not inflamed or ulcerated. The halfpence had remained there for some considerable time, forming a pouch by their pressure, but had not irritated the stomach in such a manner as to produce inflammation or ulceration." His report has been followed by others, at first, as one might suspect, mainly from Germany. These early cases were noted at autopsy and, although many were reported in full and with suggestions as to etiology and reasons for their position, they were incidental findings. They have been found at all ages. Broman [29] and Pernkopf [71] each found one in an embryo and Sinclair [73] reported a four months old child who was operated upon for the same condition. The majority of these cases were first observed when the patients were in their thirties, forties and fifties. It has been the habit of most observers to state that the abnormality was most commonly seen in women. Of the 103 cases reported, 54 occurred in women.

Description of the Abnormality

There are two general types of diverticula of the stomach.

1. *Pulsion:* This includes the congenital group and also the cases which result from such congenital malformations as a gastric muscle hiatus, a localized absence of gastric muscle, or simply a local weak area of gastric muscle. In the latter sub-division, a sufficient increase of intragastric pressure might distend the weak spot until a pouch or diverticulum was formed.

2. *Traction:* This includes such pouchings, folds, protrusions, niches, etc., as are brought about by disease process (infections, neoplasm) in the gastric wall, or by any process without the gastric wall which will cause it to protrude in any of the conditions noted above.

The diverticula reported in this paper were all of the pulsion type.

Position

The most common location for the pulsion type of diverticulum is near the cardiac opening of the stomach. Most anatomists state that in this region the stomach musculature is poorly developed.

TABLE II

Tabulation of Some of the Characteristics of 103 Uncomplicated Pulsion Diverticula of the Stomach

	Intact	Thinned Muscles	Mucosa and Serosa only	No Note	Cardiac	Lesser Curvature Mid Portion	Lesser Curvature Pre-pyloric	Greater Curvature Mid Portion	Greater Curvature Pre-pyloric	Miscel.	Male	Female	Not Stated	Present	None	Questionable	No Note
Condition of Wall of Diverticulum	16	23	6	8													
Position of Diverticulum					63	11	14	5	4	6							
Sex of Patient											43	54	6				
Symptoms														50	16	16	21

From table 2 it is evident that 61 per cent of the diverticula of the stomach are situated within the radius of a few centimeters of the cardia. The other 39 per cent are distributed most frequently along the lesser curvature. They have also been found to occur along the greater curvature and on the anterior and posterior surfaces of the fundus of the stomach. In the living case reported in this paper, and in which the diagnosis was made by roentgen-ray, the diverticulum was situated on the lesser curvature some distance below the cardiac orifice.

Histology of the Walls of the Diverticula

Diverticula of the stomach may be classified under three headings in respect to the construction of their walls:

1. Those consisting of one or more layers of gastric tissue,
2. Those consisting of gastric tissue plus pancreatic cells,
3. Those consisting of tumor cells plus more or less gastric tissue.

1. *Various Gastric Layers:* In far the greater number of diverticula the stomach walls contain only gastric tissue. From case to case there may be a wide range of difference in the construction of the individual wall, it may consist of anything from gastric mucosa with a covering of serosa to a wall which includes normal muscular and mucosal layers. In table 2 the construction of the wall has been tabulated as intact, muscle thinned with mucosa and serosa present, and mucosa and serosa only. Of the 56 cases in which the diverticulum was examined and described 16 had intact walls, 23 had thinned muscular layers, and six had walls which consisted of mucosa and serosa alone. The other eight were not described.

No case has been included in which the serosa had been distorted to the extent that the diverticulum might be of the traction type. The two diverticula found in embryos were found to be lined with normal mucosa and to have a musculature like that of the rest of the stomach. This was also true in the case of the infant of four months upon whom Sinclair operated. In two of the cases in my series there was a complete absence of musculature over part of the diverticulum. This was demonstrable macro- and microscopically.

A number of investigators have endeavored to further define the characteristics of the two sub-groups (congenital and acquired) of the simple pulsion type. They would classify as congenital those which contain all the layers of the gastric wall. Those which contained thinned musculature, they would classify as acquired. Several of them believe that those whose walls consist of mucosa and serosa only should be called herniations.

It is noteworthy that although there is a great variation in the thickness of the gastric musculature, the mucosa has been found, with one or two exceptions, to be similar to that noted over the remainder of the stomach.

2. *Pancreatic Inclusion:* One case of this type is presented in my series

and 14 * others have been culled from the literature. In only one instance was such a diverticulum found near the cardia; in this patient [7] there were two diverticula, one as noted and the other near the pylorus. In the other patients the pouch was near the pylorus and (except in three instances) on the lesser curvature. The wall of these diverticula always consisted of the normal gastric layers and the island of pancreatic tissue was usually found at the peak. There seems little doubt that these represent congenital abnormalities. Broman [29] feels that they are simply the dilated excretory ducts of hypertrophied pancreatic islands whose acini have not been able to develop normally.

The only two cases which were found at operation were reported in a general article by Moynihan.[67] The finding was accidental, for he was operating for duodenal ulcers. All the others were noted at autopsy. My case is the only one reported in recent years.

3. *Tumors Benign or Malignant:* Adenomyoma [59, 91, 49, 74] have been found in the walls of gastric diverticula on four occasions, carcinoma [40, 31, 38] thrice and fibrosarcoma once.[91]

Size and Shape of Diverticula

As might well be suspected, the diverticula are of various shapes and sizes. The openings may be small and lead through a narrow pedicle into a considerably enlarged sac. Again the diameter of the opening may be the largest dimension, so that the diverticulum assumes a pouch-like appearance. If the sacs do not retain barium, the diverticula will, of course, be undiagnosed roentgenologically, and they may well be missed at operation. The diameters of the sacs of the original cases herein reported vary from 1 by 2 cm. to 5 by 6 cm. This corresponds to the variations of most of the reported cases, although some of them are larger.

The largest was measured by Stolz and Hickel [48] as 8 by 10 by 20 centimeters. It was removed at operation. Kleine [12] also reported an operative case with a diverticulum the size of his fist. In both, the walls were reported as normal and the pedicle was inserted in the prepyloric region.

Two groups of investigators [80, 84] cite instances in which small openings of gastric diverticula were seen via the gastroscope.

Roentgenologic Diagnosis

Since the use of roentgen-rays for diagnosis of gastric abnormalities, there has been a marked increase in the number of reported cases of gastric diverticula. It is in the past 15 years that the majority of the cases have been described. From the early days attention has been called to the difficulty of making the distinction between the pulsion and the traction diverticulum and especially Haudek's niche.

* Thelemen,[24] Glinski,[19] Klob,[6] Gegenbauer,[8] Wagner,[7] Nauwerk,[39] Falconer,[26] Weischelbaum,[9] Vigi and Gamberini,[53] Müller,[21] Moynihan,[67] 2 cases, Heubel,[10] Gardiner,[25] Merkel,[23] 2 cases.

It is interesting to note that the first roentgen-ray demonstration of gastric diverticulum was by Brown [35] in 1916. Before operation it was considered to be the defect of a gastric ulcer. At operation it was recognized as a pouch-like diverticulum and was invaginated. Four years later Mellon, et al.[40] noticed a defect which was called carcinoma. At operation a diverticulum was found; and section of its mucosa, they state, showed precancerous changes. It was in 1923 that Akerlund [42] elevated the technic of roentgenologic diagnosis of this condition to its present high plane. Now, under properly controlled conditions, an experienced observer is not apt to label some other condition as a diverticulum. Failure is more liable to occur on the negative side; i.e. diverticula when small, or in unusual positions may not produce recognizable shadows.

Akerlund laid down certain essential requirements to be met before a clear cut decision could be made. The sac must be mobile, it must be loose and unattached to extra-gastric surrounding tissue and organs, the shadow must be well defined, smooth, regular and must be noted from various angles. Generally there is no tenderness.

The cardiac end of the stomach is a loose, rather flabby tissue and occasionally it overlies the fundus, so that to the inexperienced observer the bizarre examples of juxtaposition are puzzling. This type of residual must not be confused with diverticula. It is possible that this is one of the bases for a number of alleged mistaken roentgenologic diagnoses of diverticula of the stomach. I say allegedly mistaken because their absence was inferred from the fact that they were not found at operation. However, as noted in the case report, it seems quite likely that some of the pouch-like type of diverticula may easily be missed at operation, particularly so when they occur in such surgically inaccessible regions as near the cardiac orifice of the stomach.

In spite of the fact that a number of roentgen-ray diagnoses have been corroborated at operation and that numerous undiagnosed diverticula have been seen at autopsy, there is a large school of skeptics. The first of these was de Quervain.[34] He has been followed by Schlesinger,[37] Guillot,[32] Zoltam,[66] Müller [38] and a number of recent Italian investigators. Especially vehement among them are Anziolotti,[51] and Taddei.[47] The former has written a long review on the subject which contains much of interest and a great deal not germane. It would seem that the only justification for this school is that it draws attention to the care necessary for diagnosis. It also illustrates the need for correct historical approach since its exponents are unaware of the proved cases in the literature.

Symptoms

Many investigators have reported instances in which symptoms were accredited to gastric diverticula. In a number of these studies, diagnosis was made by roentgen-ray. While under properly controlled conditions this is

a satisfactory procedure, it does not rule out other complicating factors which might readily be the basis for the symptoms. Other cases have been reported in which operative procedures have been carried out on patients with definitely known complicating disorders. In some of these instances the diverticulum was found during the routine surgical examination of the stomach.

The only acceptable method for establishing a basis for the belief that diverticula might cause symptoms is by surgery. In uncomplicated cases the disappearance of symptoms, following diverticulectomy, would be fairly conclusive proof if a sufficient number of patients were operated upon. In table 3 is a compilation of the 28 operations performed on patients with ap-

TABLE III

Records of Some of the Findings on 28 Patients before and after Operation

Ref.	Author	Age of Patient	Symptoms	Position of Diverticulum	Result
12	Kleine	adult	+	prepyloric	not stated
73	Sinclair	4 months	+	prepyloric	cured
44	Tupper	43	+	prepyloric	cured
56	Southerland	51	+	prepyloric	cured
27	Jones	33	+	prepyloric	cured
57	Weiss	49	+	prepyloric	cured
35	Brown	27	+	prepyloric	cured
40	Mellon et al.	54	+	greater curvature mid portion	cured
83	Gile	7	+	prepyloric	
87	Bell and Golden	37	?	cardiac	not found
63	Lawson	50	no	cardiac	not found
33	Boreszeky	32	+	prepyloric	cured
33	Boreszeky	53	+	prepyloric	cured
61	Thomson	45	+	cardiac	questionable
72	Pansdorf	48	+	prepyloric	cured
13	Kolaezek	45	+	prepyloric	
82	Lenarduzzi	48	+	greater curvature mid portion	not found
90	Bonnet	44	+	cardiac	cured
91	Rivers	36	+	cardiac	cured
		28	+	cardiac	no note
		43	+	greater curvature mid portion	no note
		30	+	prepyloric	no note
		26	+	prepyloric	cured
		51	+	prepyloric	no note
		49	+	prepyloric	cured
		59	+	prepyloric	not cured
55	Delherm	adult	+	prepyloric	cured
48	Stolz	48	+	prepyloric	cured

parently uncomplicated gastric diverticulum. It shows that an impressive number, 64.3 per cent, became symptom free after operation. Three of the operators were unable to locate the diverticulum. In 18 per cent of the cases where symptoms were accredited to the abnormality, no note was given as to the effect of the operation. In the cases of only two of the patients was there doubt that the symptoms were caused by the diverticulum. In all but six of these cases the diverticulum was located in the fundic or pyloric regions.

In a few cases, notably those of Hurst and Briggs,[54] symptoms disappeared after the patients learned to empty their diverticula by postural drainage. Bell and Golden [87] also state that this procedure might be of assistance.

Judging from the reported cases, the symptomatology is varied and apt to be vague. The most general complaint is indigestion; i.e. gas, distention, eructation and, at times, pain coming on some time after meals. A considerable number of the patients complained of a gnawing sensation and a hunger pain with relief by food which was suggestive of peptic ulcer.

Since it may now be taken for granted that diverticula do cause symptoms, it is quite likely that the symptoms of a number of those patients, whose diagnosis was made by roentgen-ray, were caused by the diverticulum. Many of the cases were carefully studied, and an analysis of the impressions of the investigators shows that in 49 per cent of the cases the opinion prevailed that there was a direct connection between symptoms and sac, and that in 16 per cent of the cases such a connection was held to be questionable.

In table 2 it may also be seen that in 21 cases (about 20.3 per cent) there was no statement as to symptoms and in only 16 cases (about 15.5 per cent) did the writers explicitly state that there were no symptoms. Of the former, 17 were noted in autopsy material in which the diverticulum was an incidental finding and a careful review of the clinical symptoms was not given. Of the latter there are a number of cases diagnosed by roentgen-ray in which the diverticulum was also a chance finding.

Bleeding is not a rare complication, having been noted on eight occasions.[56, 91, 90, 35, 42, 83, 73, 30] Surgery has been utilized in six of them. In one, evidence of bleeding from a diverticulum was found post mortem. In the other instances it ceased.

It should also be noted that in all the literature no case of rupture of a gastric diverticulum has been reported.

Miscellaneous Details

It may be of interest to recount some of the other peculiarities met with in this abnormality. Four times [91, 56, 45, 82] it has been noted that there were two or more diverticula of one stomach. In the same number of instances [42, 26, 91, 14] it has been associated with a diverticulum of the duodenum: on three [14, 82, 91] occasions a gastric diverticulum was noted in patients with diverticula of the colon.

The combination of diverticulum and ulcers has been commented upon by a number of writers. Kleine,[12] Boreszeky,[33] Schlesinger [37] and Jones [27] feel that diverticula may result from a gastric ulcer when internal pressure reaches a certain height. However, the great majority of diverticula have not been found in association with ulcers. Consequently, whereas the symptoms of uncomplicated gastric diverticula are often suggestive of peptic ulcer, it must not be forgotten that ulcers may be associated with the ab-

normality. In the articles reviewed the association of diverticulum of the stomach and peptic ulcer has been encountered 10 times.[57, 88, 37, 42, 91, 48, 12, 14] Three of the cases were reported by Kleine.[12]

Treatment

Treatment of this abnormality, as in most medical problems, is a matter of judgment. Probably a number of diverticula have been observed in the study of a patient suffering from neurosis, though the defect was giving no symptoms. The living case reported above is an example of this situation and it would be clearly erroneous to consider this abnormality as a cause of his symptoms. It is questionable if diet or medication has any useful field of application here. However, in certain instances, where there is reflex irritability, some relief may be obtained by smooth food and by belladonna. Obviously, if there are no symptoms the conditions should be left alone, for let it be recalled that no report of perforation has come to light. Consequently, there is no necessity to make an immediate decision between medical and surgical treatment.

The question of carcinoma developing is of course to be considered. Here it may be restated that only a minimal number of such cases has been observed. Therefore the risk is apparently but slight. Instances have been reported in which relief from symptoms was produced by postural drainage, but this procedure would be of service only in those cases having a sufficiently broad pedicle.

As noted above, 24 cases have been reported in which the symptoms of the patient have justified operation and in which postoperative relief was obtained. Consequently one should not hesitate to use surgery if the occasion warrants it.

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A STUDY OF FOUR CASES OF ACQUIRED ARTERIO-VENOUS FISTULA BY MEANS OF THORO-TRAST ARTERIOGRAPHY *

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ARTERIOGRAPHY is a valuable adjunct to the methods of investigation of vascular disease of the extremities. Thorotrast,† a 25 per cent stabilized colloidal solution of thorium dioxide, is a very satisfactory medium for this procedure. This radiopaque contrast medium was used first for hepatosplenography.[1, 2] It has been used without apparent serious immediate or remote ill effects by a number of investigators in this country [3, 4, 5] in spite of its non-acceptance by the Council on Pharmacy and Chemistry of the American Medical Association.[6] For several years it has been used extensively both abroad and in the United States for arteriography of the extremities.[7, 8, 9, 10, 11, 12, 13] The amount necessary for arteriography is much less than the 75 c.c. often employed for hepatosplenography. The use of this amount for the latter purpose in most of 175 cases by Rigler, Koucky and Abraham [5] over a period of three and a half years and in 200 cases by Yater, Otell and Hussey [14] over a period of nearly five years has not been found to be associated with latent radioactivity, the most important ill effect contemplated. For roentgenographic demonstration of the vascular system of an upper extremity an average of 10 c.c. and of a lower extremity an average of 20 c.c. are usually sufficient. These relatively small amounts are certainly devoid of any possible latent ill effects.

TECHNIC OF ARTERIOGRAPHY

With a moderate amount of experience the brachial artery in the antecubital fossa (the needle pointed toward the axilla) and the femoral artery in Scarpa's triangle (the needle pointed toward the pelvis) can readily be entered through the skin with a venipuncture needle (18 gauge, 2 inches long). The skin and tissues around the artery are first anesthetized under aseptic conditions with some local anesthetic, such as 1 per cent novocaine. The artery is punctured by the needle attached to a syringe containing the Thorotrast, the extremity being in position for the taking of the first roentgenogram. When the point of the needle is within the lumen of the artery bright red blood flows forcibly into the barrel of the syringe and pulsates therein until the vessels proximal to the needle are occluded. In the arm the cuff of a sphygmomanometer is usually used for this purpose, the cuff being inflated above the systolic pressure. In the thigh an assistant can

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† Manufactured by the Heyden Chemical Corporation of New York.

easily occlude the femoral artery by digital pressure of the vessel against the pubic bone. The Thorotrast, at room temperature or previously warmed, is then injected with moderate speed into the artery and the needle withdrawn. The first roentgenogram, usually anteroposterior, is taken almost at once without allowing blood to flow into the arteries.

If the upper extremity is to be studied the forearm and hand, palm upward and fingers slightly separated, are posed on one half of a 14 by 17 inch roentgen-ray film, the other half being covered by a lead shield. After the first exposure is made the extremity is shifted to the other half of the film. The sphygmomanometer cuff is rapidly deflated to the height of the diastolic pressure and four beats are allowed to pass into the forearm, after which the cuff is rapidly inflated to a point above the systolic pressure. The second exposure is then made. The first exposure usually shows the main arteries of the forearm with a few of their branches and the palmar arches; the second shows some of the main arteries of the forearm, the palmar arches, some of the digital arteries and often some of the veins.

If the lower extremity is to be studied the lower two-thirds or more of the thigh and the upper one-fourth of the leg are posed on half of the film. After the first exposure the film is shifted down to include on the unexposed half the leg and foot either in the anteroposterior position or in the lateral position with the leg somewhat flexed. Five beats are then allowed to pass into the extremity, after which the occlusion is re-applied and the exposure made. The first exposure usually shows well the femoral artery and a few of its branches, the popliteal artery and the first part of its main branches; the second shows the main arteries of the leg with some of its branches and the main arteries of the foot.

The following roentgen-ray technic is satisfactory: Tube distance 30 inches, ½ millimeter aluminum filter, high speed screens, 100 milliamperes, 2/10 second, voltage varied according to thickness of the part (3 cm., 46 K.V.P.; 4 cm., 47 K.V.P.; 5 cm., 49 K.V.P.; 6 cm., 52 K.V.P.; 7 cm., 55 K.V.P.; 8 cm., 57 K.V.P.; 9 cm., 59 K.V.P.; 10 cm., 62 K.V.P.; 11 cm., 65 K.V.P.; 12 cm., 68 K.V.P.; 13 cm., 71 K.V.P.; 14 cm., 74 K.V.P.; 15 cm., 76 K.V.P.).

One of the most important difficulties occasionally encountered is spasm of the artery consequent to its puncture. To avoid this drawback I make it a custom to inject the contents of an ampule of Spasmalgin * intravenously about 15 minutes prior to the arterial puncture. This procedure also relieves the nervous patient's apprehensiveness.

When properly performed, the injection of the Thorotrast is made with light pressure. If the injection requires undue pressure the needle is not in the lumen of the artery. Even if the medium is injected into the tissues about the artery or into the wall of the vessel, however, no serious damage

* Each ampule contains Pantopon 0.011 gm., papaverine hydrochloride 0.022 gm. and Atrinal (sulphuric acid ester of atropine) 0.001 gm. It is prepared by Hoffmann-LaRoche, Inc.

is done. There are, however, pain, redness and local heat, which subside in a very few days with the use of hot, moist compresses.

Uses of Arteriography

Arteriography has been used mainly to assist in determining the kind of vascular disease, the location of occlusions and the extent of the collateral circulation.[12, 13, 15] Consequently, most of the cases have been instances of vascular disease associated with trophic changes or gangrene. Some cases have been reported, however, of aneurysm and arteriovenous fistula. The latter have been rare. Horton has reported a case of acquired arteriovenous fistula [16] and one of congenital fistula.[17] Frieh and Levy [18] have reported two cases of the congenital form.

Acquired Arteriovenous Fistula

The acquired form is usually due to a gunshot or stab wound, more often the former. There is usually one fistula, but occasionally there are more. The penetrating body must go through both the artery and the vein. A hematoma forms about the vessels, soon stopping the hemorrhage. Adhesions develop about the outer surfaces of the vessels, closing their lateral wounds, but the blood from the artery, being under much higher pressure than that in the vein, passes through the fistula between the artery and the vein and prevents closure of the adjacent openings. Thus, the individual bleeds constantly into the veins of the extremity. The fistula is usually a direct one, the formation of an aneurysmal sac between the artery and vein being uncommon. Medium-sized and large vessels are usually affected, since the penetrating object must pass through them without completely severing them.

A small fistula is well borne by the organism, necessitating little readjustment, but a large one involving a large artery and vein calls forth compensatory mechanisms in order to overcome the effect of the constant tendency to a diminution of arterial blood volume and to provide sufficient blood flow through the affected extremity. The heart enlarges and beats faster; the pulse pressure increases, due mainly to a drop in the diastolic pressure; and the total volume of blood increases. When the fistula is closed by compression the pulse rate suddenly drops to normal (Branham's bradycardiac sign [19]), the blood pressure becomes raised, and the cardiac shadow contracts. Because of the severe strain placed upon the heart, congestive failure may eventuate.

The local effects consist in dilatation of the vein involved and the proximal part of the artery. The tributary veins become dilated and tortuous. The superficial veins of the extremity become prominent. The blood pressure in the veins of the extremity approaches that of the arteries, and the oxygen content of the blood in the veins becomes practically arterial. The veins may actually pulsate. The surface temperature over the fistula is

usually increased, that distal to it decreased. The limb distal to the fistula is often increased in girth due to venous engorgement and edematous infiltration and hypertrophy of the subcutaneous connective tissue with atrophy of the skin and skeletal muscles. Trophic changes are prone to occur distal to the fistula. Since the flow of blood through the arteries distal to the fistula is greatly decreased, the veins take over the function of the arteries in nourishing the limb, but there is difficulty in the return of deoxygenated blood from the capillaries. Partial anoxemia of the tissues results. If these tissues are even slightly injured the normal inflammatory reaction of repair is feeble or absent, and progressive ulceration or gangrene supervenes.

A loud hum with systolic accentuation is heard with the stethoscope over the fistula and in its neighborhood and is transmitted down the course of the veins, often to the tips of the fingers or toes. A thrill is palpable also over the fistula and may be transmitted a short distance along the vein.

There is usually no difficulty in differentiating between a simple aneurysm and an arteriovenous fistula, since the physical signs mentioned above are lacking except perhaps for a less intense systolic murmur, and a thrill if present is less marked. Trophic disturbances are not so common or severe. The venous phenomena do not occur, and the oxygen content of the blood in the veins is not increased.

The four cases reported below illustrate the phenomena described. They also show the value of arteriography in cases of arteriovenous fistula. The exact site of the fistula may be determined, its size estimated, and the mechanism of blood flow through the extremity explained. The extent of the collateral circulation, however, can not thus be gauged.

Case Reports

*Case 1. Small fistula between the ulnar artery and vein.** A negro boy, aged 15 years, was sent to the Gallinger Municipal Hospital on February 26, 1933 because his heart had been found to be moderately enlarged by a physician in the syphilis clinic, where he was being treated because of a positive blood Wassermann reaction. His health had always been good except for measles, mumps and chickenpox. Five months previously he had been wounded in the right arm by a shotgun. His arm had become swollen and bluish immediately afterward, but these signs had gradually disappeared without leaving any disability of the extremity. Physical examination was essentially negative except for the heart and the right arm. The heart was moderately enlarged, the apex beat being 8.5 cm. from the midsternal line in the fifth left intercostal space. There was a soft systolic murmur at the apex and a higher pitched systolic murmur at the base. The second aortic sound was accentuated. The right arm and forearm were visibly larger than the left. The length of both arms was 48 cm. The circumferences of the arms at various points were as follows: Arm, 7 cm. above olecranon process: 22 cm. left, 23.8 cm. right. Forearm just above wrist: 15.2 cm. left, 16 cm. right. Hand below thumb: 20 cm. left, 20.4 cm. right.

A number of small scars in the antecubital fossa and its neighborhood were present where the buckshot had entered. The movements of the extremity were normal. Trophic lesions and color changes were not noted, and the superficial veins were not dilated. A loud humming sound with systolic accentuation was heard with

* Previously reported by Yater and White.[20]

FIG. 1. *Case 1.* Small arteriovenous fistula between the ulnar artery and vein. Many buckshot are present in the tissues about the elbow. A small saccular bulge in the ulnar vein at the site of the fistula is shown on the ulnar side of the forearm. Arteries are visible above and below the fistula, but of the veins only the brachial is visible.

the stethoscope in the right side of the neck and down the entire length of the right arm. It was audible even at the tips of the fingers. The greatest intensity of the murmur was in the antecubital fossa nearer the ulnar side. A thrill was palpable in the extremity, but its distribution was not as great as that of the bruit. Its point of maximum intensity was much more definite than that of the murmur, being about 5 cm. below the middle of the antecubital fossa on the ulnar side. The heart rate was 80 per minute, and the rhythm was regular. The systolic blood pressure was 140 mm. Hg and the diastolic 80 mm. Hg in the left arm; in the right arm the systolic pressure was also 140 mm. Hg, but the diastolic pressure could not be determined, the sounds being heard loudly down to the zero point. Closure of the fistula by compression over the point of maximum thrill did not alter the pulse rate appreciably, but the systolic blood pressure in the left arm dropped to 130 mm. Hg. The Kahn test of the blood was 4 plus; hemoglobin, 88 per cent (Newcomer); leukocytes, 5200 per cu. mm. The urinalysis was normal. Determination of the oxygen content of the blood in the superficial veins of the right arm showed that the blood was practically arterial. A roentgenogram of the chest revealed moderate enlargement of the heart.

An arteriogram was made by injecting 10 c.c. of Thorotrast into the brachial artery at about its middle (figure 1). Because of the high puncture point a tourniquet was used instead of a sphygmomanometer cuff to occlude the vessels above. A large number of buckshot were shown in the tissues about the region of the elbow. The brachial artery and the arteries of the forearm were well demonstrated, especially the radial and the interosseous. A moderate number of smaller arteries were shown. On the ulnar side of the forearm a short distance below the elbow joint there was a small rounded shadow representing a localized saccular dilatation of the ulnar vein at the site of the fistula. The veins below this point were not demonstrable, but the brachial vein above the elbow was quite obvious. The fistula was apparently one connecting the first part of the ulnar artery and vein. The ulnar artery itself at that point could not be clearly seen because of the presence of buckshot, nor was it possible to say positively that any of the small arteries running downward from this region was the ulnar. They appeared to be more probably muscular branches of the radial artery.

Since it was thought the cardiac enlargement was due to the fistula, operation was advised but was refused. The boy was examined again three years later. He was in excellent health, and there was no appreciable change elicited in the physical examination. Operation was again refused.

Comment. Although it seemed that the increased size of the heart was due to the fistula, the fistula was undoubtedly a very small one. To begin with, the affected vessels were relatively small. There was little change in the circulatory status when the fistula was closed. The bruit and thrill of a small fistula are just as intense as those of a large one, sometimes more; so that these signs may not be used as indicators of size. The arteriographic features indicating a small fistula were (1) that the veins were not demonstrated below the sac, (2) the sac was small and localized, and (3) the arteries both above and below the fistula were well shown.

Case 2. Small fistula between the popliteal artery and vein. The patient, L. D., a negro aged 44 years, was admitted to the Gallinger Municipal Hospital on July 18, 1935, complaining of chills, fever and pain in the lower right axillary region, which he claimed had begun suddenly about 24 hours before. For about a year he had had a productive cough, increasing weakness, night sweats, low grade fever, occasional

diarrhea, occipital headaches, some loss of weight, vertigo, tinnitus, palpitation of the heart and some dyspnea on exertion. He had been shot with a shotgun in the right popliteal region in 1907. He had had pneumonia, gonorrhea, a chancre and typhoid fever. He did not appear to be very ill. Physical examination was essentially negative except for evidence of pneumonitis in the lower part of the right lung, moderate enlargement of the heart with a blowing systolic apical murmur, and the following findings in the right lower extremity. The latter was larger than the left, having a circumference about 1 cm. greater both above and below the knee. A marked systolic thrill was palpable whose greatest intensity was in the right popliteal fossa, but which was felt half way up the posterior surface of the thigh and half way down to the ankle. A loud, harsh bruit was heard with the stethoscope in the popliteal fossa and was transmitted up the posterior surface of the thigh to the back and abdomen and down the leg to the plantar surface of the foot and to the tips of the toes. This was practically continuous, with systolic accentuation. Both thrill and bruit ceased when the femoral artery was compressed above Scarpa's triangle. The blood pressure in the arms was 180 systolic and 100 diastolic. In the right thigh it was 248 systolic and 100 diastolic, while in the left it was 220 systolic and 120 diastolic. The temperature was 102° F., the pulse rate was 120 per minute and the respiratory rate was 26 per minute. Urinalysis was normal. The hemoglobin was 75 per cent; the erythrocytes numbered 3,760,000 and the leukocytes 18,000 per cubic millimeter of blood, with 63 per cent polymorphonuclear leukocytes and 18 per cent band forms. The Kahn test of the blood was negative. A roentgenogram of the chest showed a small area of opacity in the right apex and an irregular area of increased density in the basal portion of the right lung. The temperature continued to be elevated a degree or two each afternoon, but the symptoms were soon greatly relieved by bed rest. Attention was then focused on the arteriovenous fistula of the right popliteal artery and vein.

The blood pressure gradually dropped, and on July 25 it was 134 systolic and 84 diastolic in the arms, 180 systolic and 90 diastolic in the right thigh, and 164 systolic and 90 diastolic in the left thigh. With compression over the arteriovenous fistula the blood pressure rose to 148 systolic and 100 diastolic in the arms and to 170 systolic and 110 diastolic in the left thigh. At the same time the pulse rate dropped from 95 to 88 per minute. The venous pressure rose from 86 mm. to 110 mm. of water. The blood volume as determined by the Congo red test was 5800 c.c. The circulation time as determined by the saccharine test was 14 seconds. Blood from a vein in the right thigh was bright red.

Roentgenograms of the middle of the right lower extremity were made after the injection of 20 c.c. of Thorotrast into the right femoral artery in the region of Scarpa's triangle, with the artery occluded just above by the fingers of an assistant. Although the artery and not the vein was injected, as indicated by the pulsations in the syringe after piercing the vessel, and although closure of the artery above the point of injection was maintained by pressure, it was mainly the veins that were demonstrable in the films (figure 2). The femoral and popliteal veins were greatly enlarged, more especially in the knee, and just below the joint there was a saccular down-pouching of the popliteal vein. Part of the great saphenous vein was visible above the knee. The popliteal vein just below the fistula was seen and also some of its small muscular tributaries, but all were of small size and not tortuous. In the upper part of the film a few small arteries were also noted (not shown in the photograph). Some scattered buckshot were present in the tissues. On another day the injection was repeated (figure 3). The first roentgen-ray exposure was made a trifle later than on the former occasion. The appearance was essentially the same, except that the femoral vein was not visible, but the great saphenous vein, which anastomoses freely with the popliteal vein, was well shown.

On August 13 an operation was performed to remove the segment of the popliteal artery and vein including the fistula. It had been assumed that the collateral circulation was well developed because of the great age of the fistula. But in spite of all postoperative precautions gangrene of the stump followed, and the right leg was

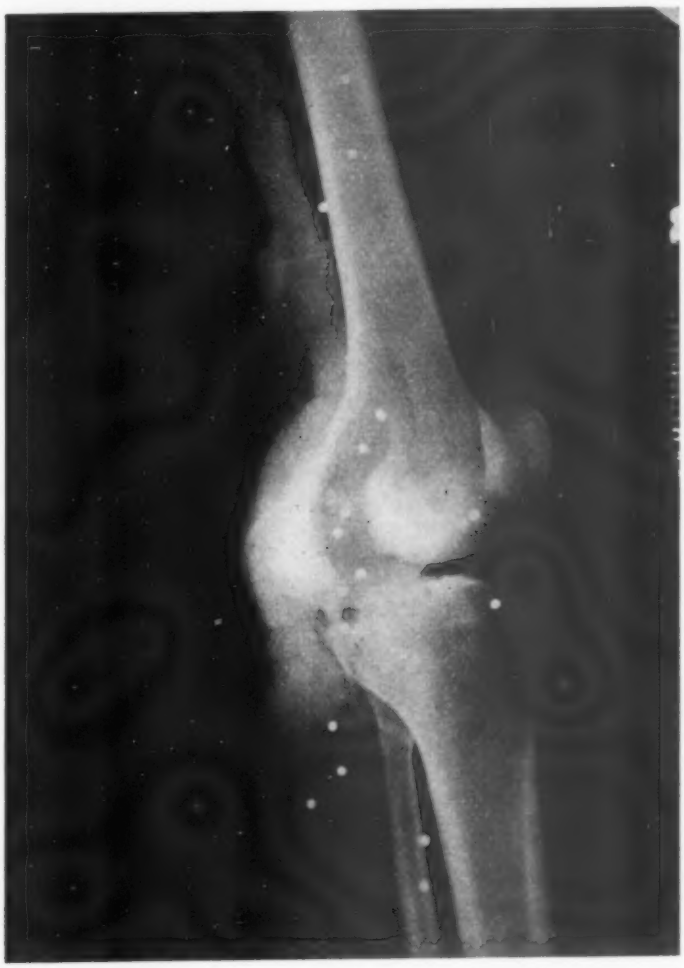

FIG. 2. *Case 2.* Small arteriovenous fistula between the popliteal artery and vein. No arteries are visible. The femoral vein is distended; the popliteal vein is greatly distended and presents a rounded saccular bulge below the knee. The part of the popliteal vein below the fistula is small. Part of the great saphenous vein is shown near the femoral vein. Buckshot are present in the tissues.

amputated above the knee on August 25. However, infection developed in the stump, followed by septicemia, and death occurred on September 21.

Examination of the segment of the popliteal artery and vein containing the fistula showed that both vessels were moderately enlarged and thickened. The fistula was small, admitting only a small probe. The venous sac which had been demonstrated in the roentgenograms was not evident in the empty vessels. Apparently it was not an anatomical sac but merely a dynamic or functional one which existed only during life.

The pulmonary condition for which the patient was hospitalized did not progress during the period of hospitalization. Actually, the pneumonitis of the right lower lobe resolved, as indicated by physical examination and roentgenograms of the chest. The patient's cough subsided but returned a few days before death. Several ex-

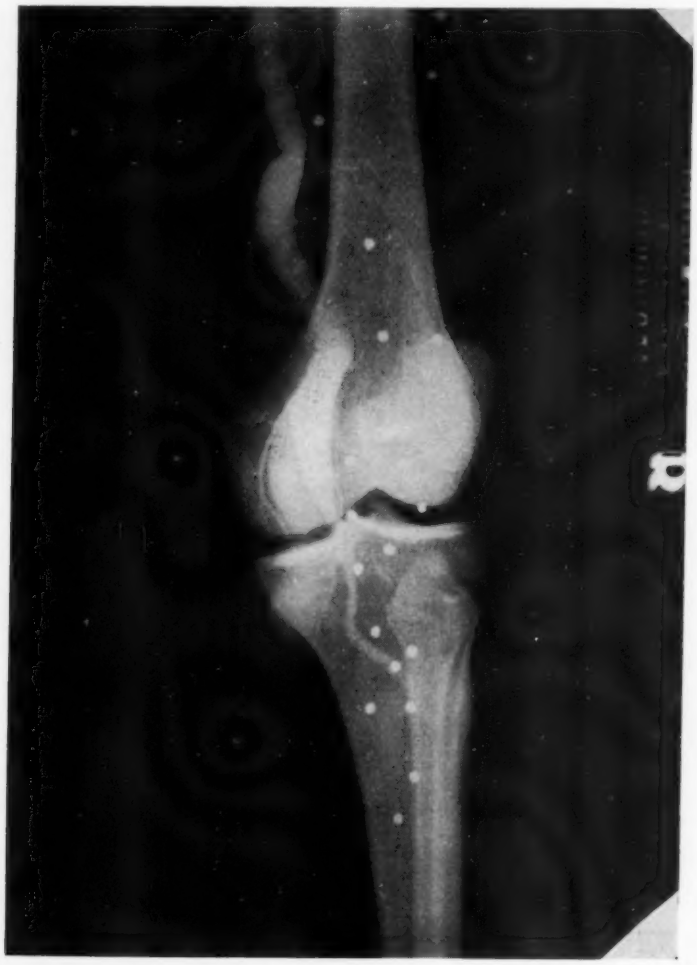

FIG. 3. *Case 2.* Another film after a second injection of Thorotrast. The contrast medium has left the femoral vein and fills mainly the great saphenous vein and the popliteal vein.

aminations of the sputum failed to reveal tubercle bacilli. Permission for necropsy could not be obtained because the patient had no known relatives.

Comment. Although the arteriograms in this case were not essential to the diagnosis of arteriovenous fistula nor to the determination of the location of the fistula, and although mistakes in judgment were made, interesting information was obtained from the experience afforded by the case. As Allen and Camp [13] have stated, arteriography is valuable in increasing

our knowledge of the mechanics of vascular diseases. In the case here reported it is seen that the force of arterial blood passing into a vein through a small opening may produce during life a localized dilatation in the vein which roentgenographically resembles an aneurysmal sac but which is not a true aneurysm. The small size of the fistula was demonstrated arteriographically by the absence of dilated and tortuous veins distal to it. The absence of arterial shadows shows how rapidly blood flows from the artery into the vein even through a small fistula, but in the case of a small fistula apparently most of the blood entering the vein through the fistula returns immediately toward the body and relatively little goes into the veins of the limb distally.

The great age of the fistula without evidence of chronic passive congestion in this case was an indication of its small size. The cardiac hypertrophy was due probably more to hypertension than to the fistula. A small fistula is not necessarily conducive to the development of an adequate collateral circulation, even after many years of existence. In fact, it is impossible on the basis of arteriographic studies to determine whether a fistula of any size stimulates the formation of a very adequate collateral arterial circulation, although in all other vascular diseases of the extremities the extent of the collateral circulation is one of the most important uses of arteriography. However, Reid,[21] on the basis of clinical and experimental studies, concluded that an arteriovenous fistula is the most powerful stimulus there is to the development of collateral circulation of the surrounding vessels. Nevertheless, it is safer to assume in any case of arteriovenous fistula that the collateral circulation is not adequate, and measures to assure an adequate collateral circulation should be instituted before operation. Such measures consist mainly in the daily occlusion of the artery leading to the fistula for a few weeks prior to operation. Increasing periods of occlusion from five to fifteen minutes one to several times a day should be instituted. Had this procedure been followed in this case the patient's limb and life might have been saved, although it is well known that ligation of the popliteal artery is frought with more danger than that of the femoral artery higher up.

Case 3. Small fistula between the femoral artery and vein. A white man, G. B., aged 34 years, entered Georgetown University Hospital on January 7, 1936, complaining of weakness, dyspnea on exertion, pallor, nocturia, and swelling of the ankles. The illness had apparently begun about 10 months before with intermittent pains in the right side of the body from the shoulder to the hip, present mainly on exertion. After several months these had ceased. Much later the other symptoms had become noticeable. The past history was unimportant except for a shotgun wound in the left thigh when the patient was eight years old. About three weeks later he had noticed a palpable thrill just distal to the left inguinal ligament. About seven years later arteriovenous aneurysm was diagnosed on the occasion of a fracture of the left hip. On admission he was found to be poorly nourished, pale and weak. The heart was slightly enlarged, and there was a loud systolic apical and precordial murmur. The blood pressure was 132 systolic and 56 diastolic. Numerous small scars were

present in the skin of the upper, anterior part of the left thigh. There were visible strong pulsations of the femoral artery in Scarpa's triangle with slight bulging in that region. A strong thrill was palpable in the same area. A loud systolic murmur was audible from the umbilicus to the tips of the toes, with greatest intensity over the femoral artery just below the inguinal ligament. There were no trophic changes, and there was very little difference in the measurement of the lower extremities. With pressure over the apparent site of the fistula the pulse rate instantly dropped from 98 to 90 per minute; the venous pressure rose from 72 to 174 mm. of water; and the blood pressure fell 10 mm. Hg. The blood pressure in the left leg was 140 systolic and 68 diastolic and in the right leg 124 systolic and 64 diastolic. The urinalysis showed some albumin and a few casts. The hemoglobin was 28 per cent (Newcomer), the erythrocytes numbered 1,980,000 and the leukocytes 6,800 per cubic millimeter of blood, with 68 per cent polymorphonuclear neutrophiles. The blood non-protein nitrogen was 45 mg. per 100 c.c. of blood. The phenolsulphonephthalein test of renal function showed 12 per cent elimination of the dye during the first hour and 18 per cent during the second hour. The Kahn test of the blood was four plus. The temperature was elevated irregularly daily to 101.5 to 103° F. with occasional morning remissions to normal. The pulse rate varied from 100 to 130 per minute.

An arteriogram was made with some difficulty, since the fistula was apparently so high in the thigh that the femoral artery had to be injected close to the inguinal ligament and therefore close to the point where the assistant occluded it. Furthermore, firm compression at this point was quite painful. However, a fair arteriogram was obtained (figure 4). Shadows of many buckshot were seen in the tissues of the upper thigh. There were no arteries definitely visible. A large, somewhat oval and mottled shadow of the dilated upper part of the femoral vein was visible. Below this on the medial side of the femur were the main vein and a moderate number of small veins, not very tortuous. On the lateral side of the femur other straight veins were evident.

Subacute bacterial endocarditis was considered a probable diagnosis in spite of persistently negative blood cultures, but on reflection it was deemed possible that the vegetations might be present in the arteriovenous fistula and not in the heart, as in the case of Hamman and Rienhoff.[22] Accordingly, it was decided to attempt extirpation of the fistula, but only after a period of daily occlusions of the femoral artery to stimulate the development of collateral circulation, even though the fistula was considered to be small and had existed 26 years without evidence of heart failure or trophic changes. During this preparatory period evidence of increasing renal insufficiency developed, the blood non-protein nitrogen rising to 70 mg. per 100 c.c. of blood.

On January 29 operation was performed by Dr. Fred Sanderson. The fistula was found to be located about 2 cm. below the origin of the profunda femoris artery, which like the common femoral artery was very large. The femoral vein was greatly dilated in this region. There were many vessels in the vicinity, mainly veins, and the operation was difficult. The segments of the femoral artery and vein containing the fistula were extirpated. In order to control hemorrhage it was unfortunately necessary to ligate the great saphenous vein, and a hemostat had to be left on a tributary vein. Examination of the specimen removed showed a fistula about 2 mm. in diameter connecting the artery and vein directly and containing no vegetations.

After the operation the arteries of the leg and foot were still felt to pulsate, and the extremity remained almost as warm as the other. However, the limb swelled a great deal and became somewhat livid because of venous obstruction. The day following the operation a diastolic murmur became audible over the base of the heart for the first time. A day later petechiae first appeared. Hiccough began and persisted. The operative wound became infected. Ten days after the operation profuse venous hemorrhage occurred from the wound, and a few hours later the patient died.

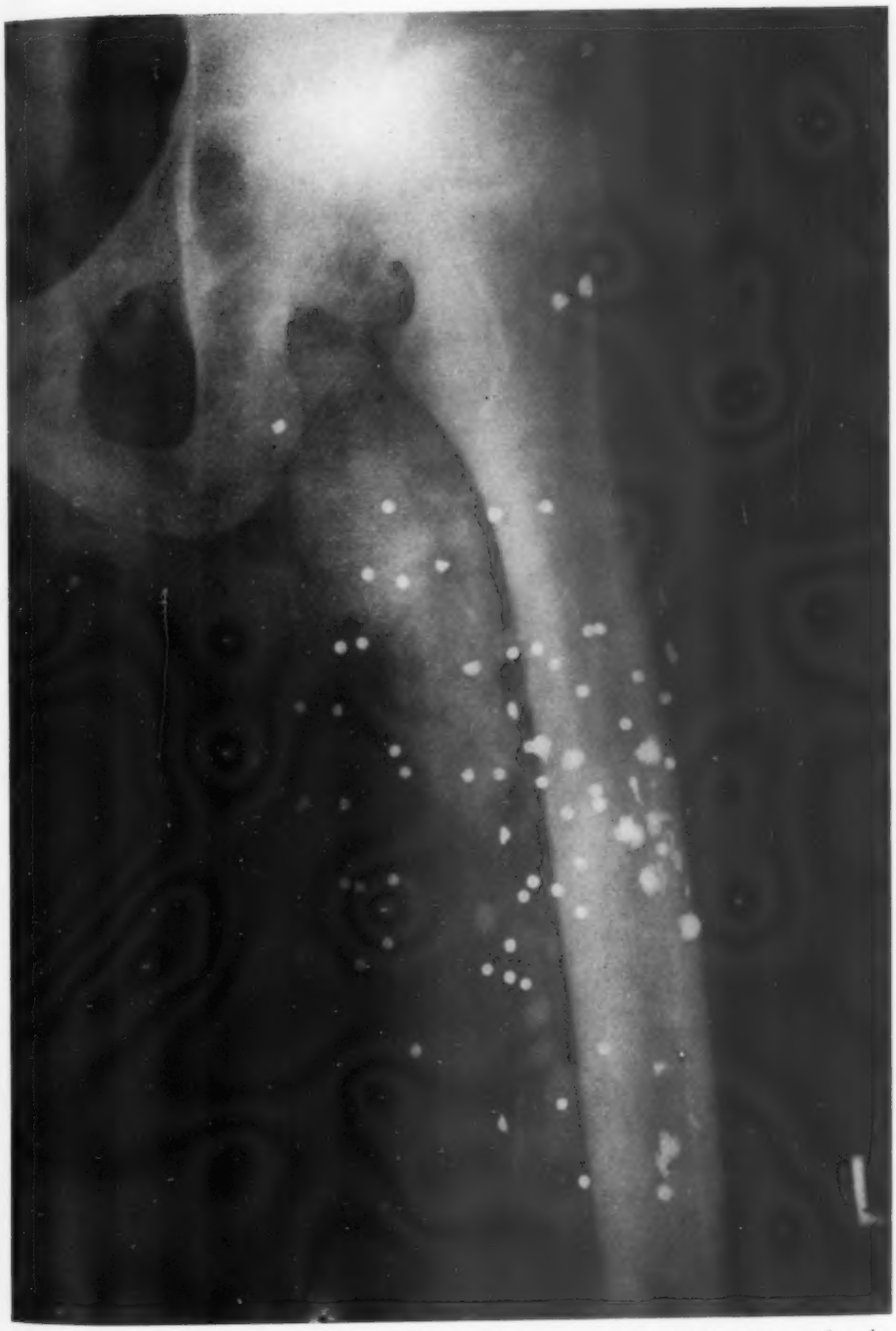

FIG. 4. *Case 3.* Small arteriovenous fistula between the femoral artery and vein. No arteries are visible. The upper part of the femoral vein is greatly dilated. Below this fusiform venous aneurysm the veins are visible but are not tortuous. Many buckshot are present in the tissues.

Necropsy revealed bacterial vegetations on the aortic valve but no evidence of chronic endocarditis. The femoral vein was completely thrombosed. There was ulceration of the profunda femoris artery, and a small communication with the vein had resulted from this lesion.

Comment. The fistula was small and had existed for years, but some part of the arterial blood to the affected extremity apparently passed into the veins through the fistula, although a goodly part also went down the profunda femoris artery. The direct course of the veins instead of a tortuous one indicated that the fistula was small. If it had not been necessary for controlling hemorrhage to tie the great saphenous vein the fistulectomy would undoubtedly have been successful, since the fistula was just distal to the origin of the profunda femoris artery. However, the venous return was obstructed and thrombosis occurred in the veins, resulting in severe venous stasis in the limb. The foot remained warm and the arterial pulsations were present.

*Case 4. Large fistula between the popliteal artery and vein.** The patient, G. K., a negro aged 52 years, had been shot in the region of the left knee with a 0.38 caliber rifle in 1921, 14 years before. The bullet entered the skin just below the patella on the anterolateral aspect of the leg and came out in the lower popliteal region. In three or four days the leg became greatly swollen from the knee down. It had remained almost as large from that time but was always less swollen after a period of bed rest. An ulcer had appeared about a year later on the middle of the anterior aspect of the leg. This had become quite large but some healing had occurred from time to time. The toe nails of the left foot had become thickened and had not grown as fast as those of the right foot. For the previous five years there had been intermittent bleeding from the rectum of variable amounts of bright blood. Some dyspnea on exertion had been noticed latterly.

The essential points of the physical examination were as follows: The heart was moderately enlarged, the visible apex impulse being 10.5 cm. from the mid-sternal line (the clavicle measured 18 cm.) There was a systolic precordial murmur. A strong pulsation synchronous with the heart beat was palpable in the left lower quadrant of the abdomen. The left leg was considerably larger than the right below the knee. The measurements were as follows:

Circumference, middle of thigh, right—43 cm., left—41.8 cm.
Circumference of calf, right—31 cm., left—37.3 cm.
Distance from anterior superior iliac spine to internal malleolus, right—97.5 cm., left—100 cm.

A large area on the anterior and lateral surfaces of the left leg was deeply pigmented, and there was a small, irregular granulating ulcer in its middle (figure 5). The left ankle was limited greatly in its movement. The left foot was red, very moist and quite warm. The superficial veins were prominent over the left thigh and upper calf, and the great saphenous vein was very large (about 2 cm. in diameter) from just below the knee up nearly to Scarpa's triangle (figure 6). Blood drawn from this vein was as red as arterial blood. The femoral artery was seen to pulsate extremely in the upper part of the thigh, and could be occluded with the fingers with difficulty. The popliteal artery also pulsated greatly. A strong thrill was palpable in the popliteal fossa and radiated upward and downward for several inches. A very loud, almost continuous bruit with systolic accentuation was audible with greatest

* Case of Dr. Paul Putzki at Providence Hospital.

intensity in the popliteal fossa, but could easily be heard down to the tips of the toes and up to the umbilicus.

The pulse rate was 92 per minute, and on occlusion of the popliteal artery by compression it dropped immediately to 64 per minute. The blood pressure in both arms was 130 systolic and 60 diastolic with the fistula open and 150 systolic and 80

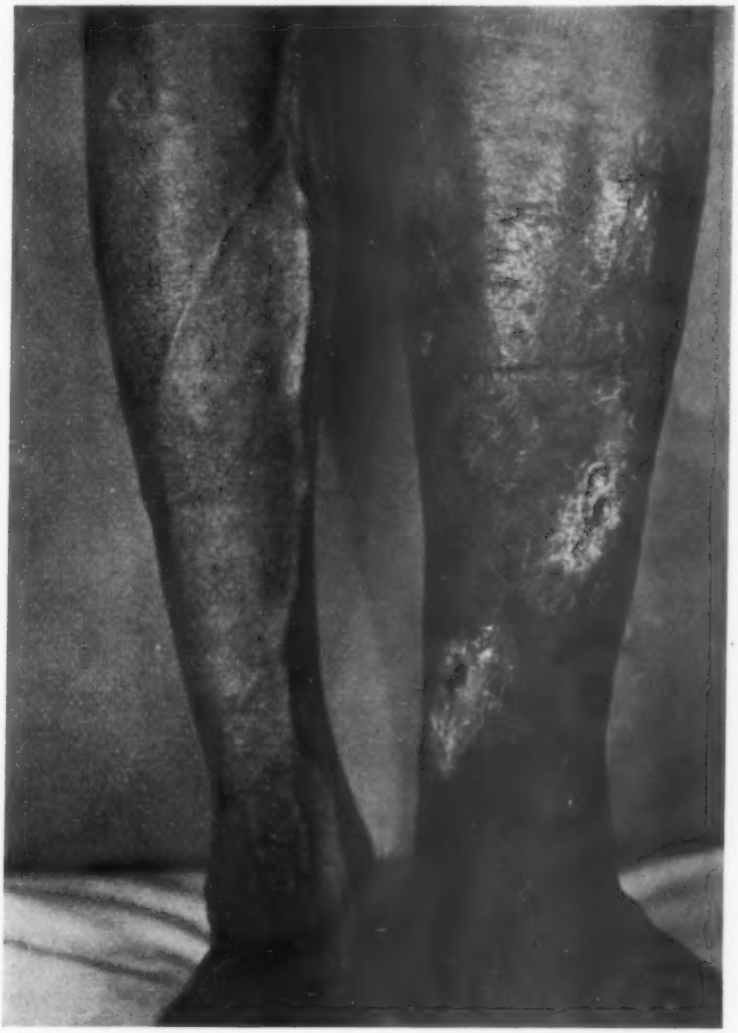

FIG. 5. *Case 4.* Large arteriovenous fistula between the popliteal artery and vein. Affected leg enlarged, pigmented and ulcerated.

diastolic with it closed. The blood pressure in the left thigh was 300 + systolic and 60 diastolic. In the right thigh it was 190 systolic and 120 diastolic with the fistula open and 220 systolic and 130 diastolic with it closed. The venous pressure in the right antecubital vein was 68 mm. of water with the fistula open and the same with it closed. In the right saphenous vein it was 84 mm.; in the left it was 160 mm., and

the column oscillated with the heart beat. The circulation rate with the saccharin test was 31 seconds when the fistula was open and 23 seconds when it was closed. Thermographic studies showed an increase of temperature of the skin in the left popliteal space, but very little change elsewhere in the affected limb.

Studies of the rectum did not reveal any intrinsic lesion, and it was thought that

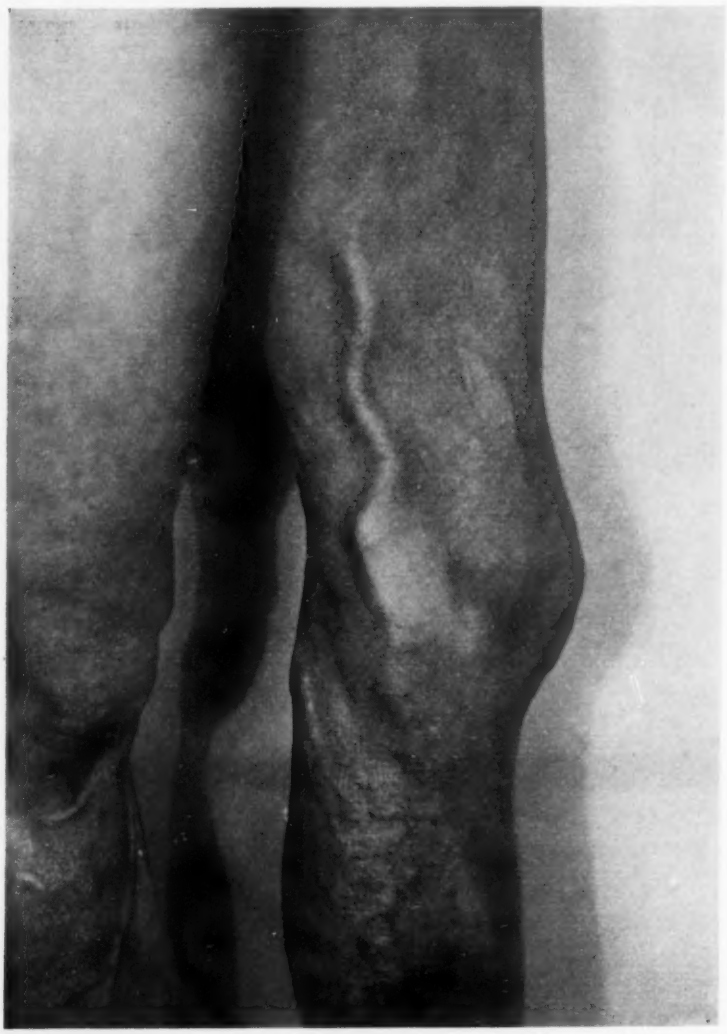

FIG. 6. *Case 4.* Great saphenous vein greatly dilated.

the pulsations in the left lower quadrant of the abdomen were due to dynamic pulsation of the iliac artery on that side and that the bleeding was due to venous engorgement about the rectum.

Two series of arteriograms were made on different days. The first time 25 c.c. of Thorotrast were used, but due to the large size of the venous bed in the extremity the shadows were not as dense as usual. The second time better detail was shown by the injection of 50 c.c. Several films were taken in succession as rapidly as pos-

sible, one beat being allowed to go down the limb between films (figures 7 to 10). The only arteries visible were some small ones high up in the thigh. In the first film the popliteal vein was seen to be greatly distended and some of its tributaries filled; the great saphenous vein with one of its branches was visible (figure 7). In the second film the popliteal vein appeared to be even larger and more of its tributaries

FIG. 7. *Case 4.* Large arteriovenous popliteal fistula. Film number 1 of a series. The popliteal vein is greatly dilated and forms a pouch below the knee. The great saphenous vein is visible. Tributary veins are very tortuous.

in the leg were visible, resembling large round worms; there was also a long, coiled vein in the thigh, but the saphenous vein was no longer evident. The third film was essentially the same, but the veins in the calf were more prominent (figure 8). In the fourth film there was just a dim shadow of the popliteal vein, but the veins in the calf were very numerous, and more small veins were visible in the thigh (figure 9). The fifth film showed the small veins very indistinctly, but the femoral and saphenous

FIG. 8. *Case 4.* Film number 3. The great saphenous vein is no longer visible. Many coiled veins are visible below the knee.

veins were visible, although they were not as dense as originally (figure 10). The sixth film was quite similar. The roentgenograms also showed enlargement and evidence of osteitis of the tibia and fibula.

The patient was kept in the hospital several weeks and daily occlusion of the femoral artery performed. The leg became smaller and the ulcer healed. Before operation was contemplated the patient secretly left the hospital.

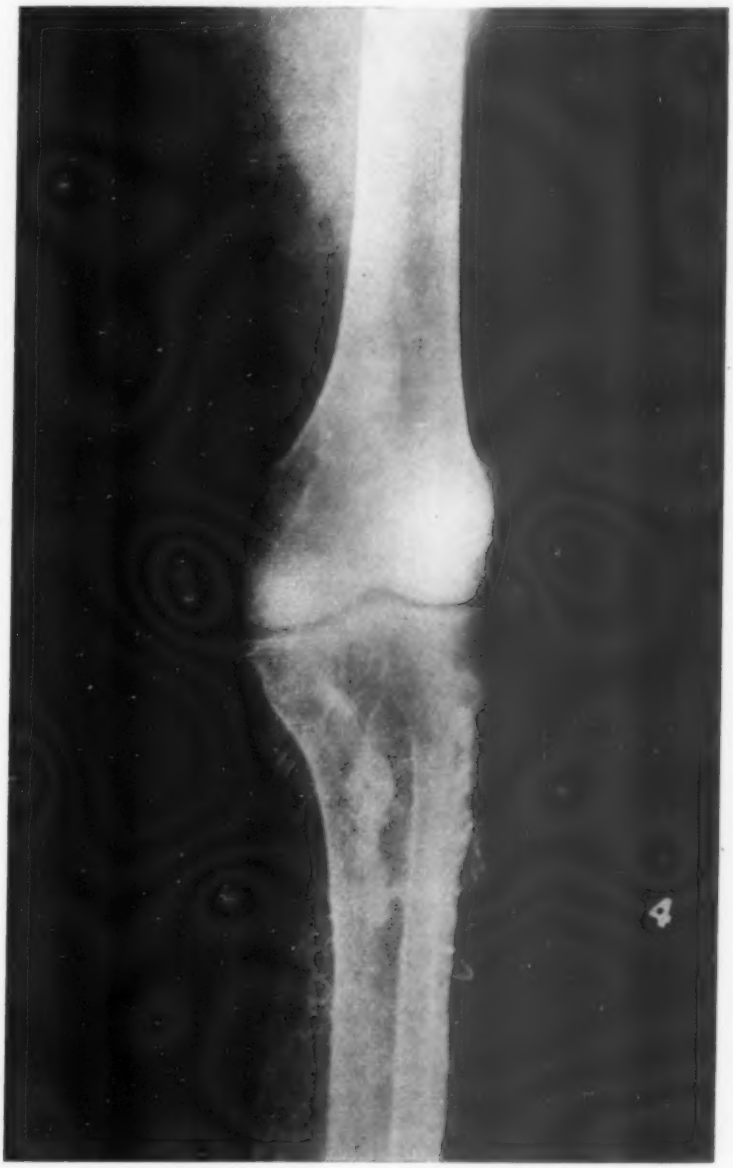

FIG. 9. *Case 4.* Film number 4. The veins in the thigh are barely visible. Those in the leg are still readily apparent.

Comment. This was a case of a large fistula which had existed 14 years without congestive heart failure. Trophic changes were prominent. Practically all of the blood below the knee went through the veins, which ap-

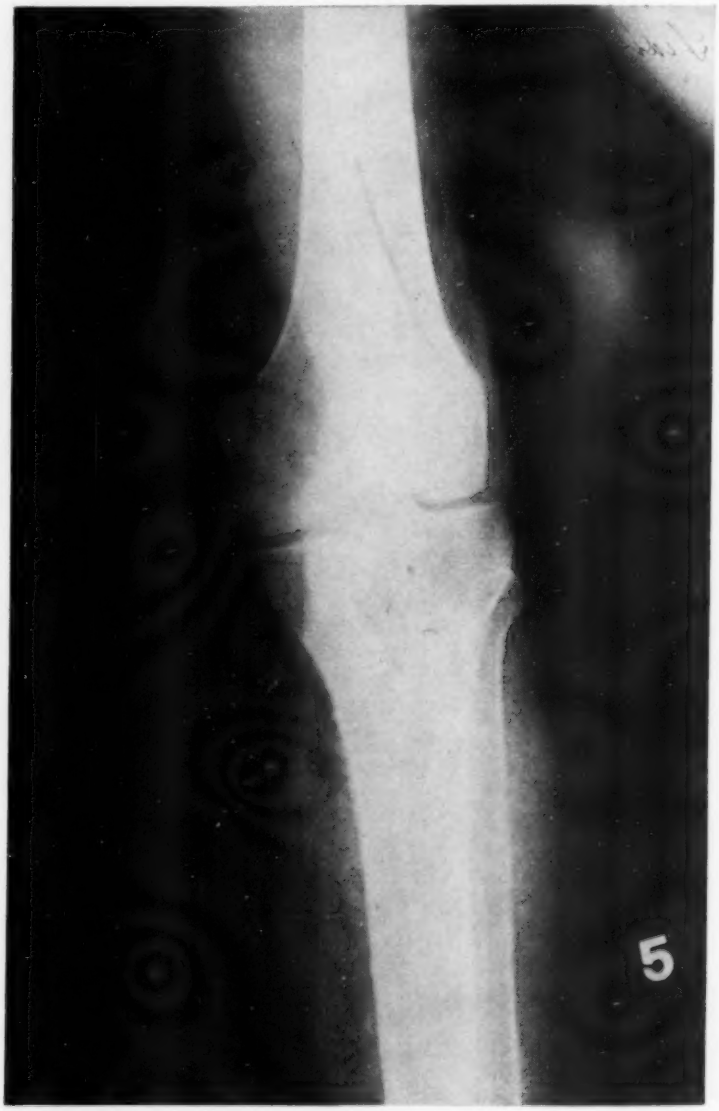

FIG. 10. *Case 4.* Film number 5. The popliteal and great saphenous veins are again evident. The veins below the knee are barely visible.

parently assumed the function of arteries in nourishing the tissues. This function was insufficient because of difficulty in the return of deoxygenated blood from the limb. The arteriograms indicated that the deoxygenated blood left the leg slowly by the same veins through which it entered. Ap-

parently there were two simultaneous, opposite currents in the veins below the fistula.

Conclusions

The following points may be determined by arteriography in cases of arteriovenous fistula: (1) the site of the fistula, (2) the size of the fistula, and (3) perhaps the mechanism of the circulation in the limb below the fistula.

The site is indicated by the point of greatest bulge in the affected vein, which frequently just below the fistula forms a rounded saccular pouch.

The size of the fistula is shown by the degree of visibility of the arteries in the films, by the size of the large veins, and by the number and tortuosity of the smaller veins, particularly those distal to the fistula. In cases of small fistula the arteries may be visible and there are no or relatively few veins visible below the fistula. The few small veins that may be visible are not tortuous. Even in the case of a small fistula between larger vessels the arteries may not appear in the films. In cases of large fistula the arteries are probably never visible, but the large veins are prominent, and the small veins, especially those distal to the fistula, are enlarged, seemingly increased in number and very tortuous.

When the fistula is large the veins distal to the fistula must assume the function of arteries. The return of deoxygenated blood from the limb below the fistula apparently occurs through the same veins down which the arterial blood passes.

The extent of the collateral circulation in cases of fistula is very difficult to judge from arteriograms, since with larger fistulae the arteries are not visible. It is safest to assume in every case of arteriovenous fistula that the collateral circulation is not sufficient and to institute measures to assure an adequate collateral circulation before the operation is performed. In arterial diseases of the extremities, on the contrary, the extent of the collateral circulation can be rather accurately determined by the aid of arteriography.

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EFFECTS OF GASTRIC AND INTESTINAL HYPERPERISTALSIS ON THE ELECTROCARDIOGRAM AS DEMONSTRATED BY SIMULTANEOUS MECHANOGRAMS AND INDIRECT AND SEMIDIRECT ELECTRIC LEADS *

By I. Harrison Tumpeer, S.M., M.D., *Chicago, Illinois*

Registration of gastric and intestinal hyperperistalsis on the electrocardiogram has been reported in a previous study.[1] The sources were the gastric activity in a baby with congenital hypertrophic pyloric stenosis and the intestinal contractions in a child with congenital hypertrophic dilatation of the colon (Hirschsprung's disease), and in an elderly adult in whom borborygmi occurred in the course of a routine electrocardiogram. Hyperperistalsis was visible in the first two conditions and audible in the last.

The peristaltic effect upon the electrocardiogram is not even considered in such a review as Esler and White's [2] nor is it mentioned in Mortensen's [3] study of abnormal electrocardiograms. The influence of such smooth muscle activity seems entirely ignored although suggestive effects are present in some of Wenckebach and Winterberg's [4] observations on the effect of vagus pressure and in a group of routine tracings from the Heart Station of Michael Reese Hospital examined by the author. Alvarez and his coworkers [5, 6, 7] have reported electrical registration of peristalsis in man and animals. In the latter simultaneous mechanograms were submitted. Richter [8] has demonstrated electrogastrograms of the exposed stomach in etherized dogs, and more recently Hasama [9] studied the pendulum peristalsis in the small intestines by direct electrodes. Puestow [10] worked with isolated intestinal loops and muscle strips obtaining electrical and mechanical records. Berkson [11] as well as Puestow demonstrated that these effects maintain their relationship even after the tissue has been isolated from the central nervous system, indicating an intrinsic mechanism controlling peristalsis. Nevertheless, no previous observations on simultaneous electrical and mechanical phenomena have been demonstrated in the intact human subject. The present study was undertaken to record objectively the simultaneous mechanical and electrical registrations during gastric and intestinal hyperperistalsis.

The Present Study

Gastric hyperperistalsis was studied in an adult male with pyloric obstruction and marked visible peristalsis.

* Received for publication February 6, 1936.

From the Sarah Morris Hospital for Children and the Heart Station, Michael Reese Hospital, Chicago.

With the technical assistance of Bessie Phillips, Electrocardiographic Technician, Heart Station, Michael Reese Hospital, Chicago.

Case Report

E. R., male, 42 years old, was admitted to the Michael Reese Hospital, medical service of Dr. Wm. C. Buchbinder, September 21, 1934, with the admission diagnosis of pyloric obstruction due to duodenal ulcer, and signed his own release because he refused surgical treatment, October 5, 1934. His symptoms had begun two years before with postprandial, peri-umbilical pain occurring one or two hours after meals, associated with a sensation of weakness and nausea, and more recently with vomiting at the onset of the pain. He had vomited food eaten one or two days previously. Vomiting had increased in frequency so that recently he dared not eat a meal but nibbled small amounts of food continuously. Earlier in the course of the illness the Sippy régime had been prescribed at another institution but appeared to aggravate the symptoms. One year ago baking soda had given slight relief, but in the past few months it had increased his distress by the resulting gas formation. The pain has sometimes been relieved by cold milk, and always by vomiting. He awakened three to five times nightly. He had lost seven pounds in the preceding six months and three in the preceding two weeks. For the past two months he had felt weaker, and recently had vomited practically everything; he had been continuously hungry but could not eat. There had been no bowel movement for three days before admission.

Physical examination revealed a poorly nourished, white male, not acutely ill. The chief finding was marked epigastric peristalsis with gurgling and splashing sounds when the upper abdomen was tapped. As much as 2000 c.c. of gray brown liquid were aspirated in a series of frequent gavages. The blood picture, blood sugar, non-protein nitrogen and urine were within normal limits. Blood pressure was 108 to 112 systolic and 84 to 72 diastolic.

Fluoroscopic Report: "Stomach contains a considerable amount of residual fluid. The fundus is dilated, and the walls reveal marked peristalsis. Definite antral and pyloric spasm is present. Tenderness is elicited over the pylorus. There is 80 per cent retention in five hours. The duodenal cap does not fill immediately, and is markedly defective when filled in one-half hour."

Roentgenographic report: "The film confirms the fluoroscopic findings, revealing a pyloric obstruction and a defective cap. Whether the cause of obstruction is duodenal or pre-pyloric is not revealed owing to the pronounced pylorospasm."

Study A. Lead III was taken on the patient with a slowed camera. The mechanical registration was accomplished by air pressure effects on a Frank capsule [12] to whose rubber diaphragm a tiny mirror was fastened throwing a beam of light on the slit in the camera of the electrocardiograph so that both electrical effects by means of Lead III and mechanical effects could be registered on the film simultaneously. In this part of the study the patient swallowed the usual stomach balloon which was attached by rubber tubing to the Frank mirror-holding capsule. (Figure 1).

Comment. The undulation in the base line of the electrocardiogram occurs with the passing of the peristaltic wave usually beyond the mid line. It is not an artefact and resembles the kymographic record of a peristaltic wave. This has been pointed out by Alvarez and myself. The excursions differ from the kymographic record because the rapidity of the film distorts the picture by widening and flattening the curves. The black band tracing is the result of changes in the pressure of the stomach balloon and represents only crudely, as will be explained, the mechanogram of the stomach. The

superimposed low excursions in the latter occurring about every three to four seconds demonstrate nicely the respiratory effect.

If the longer excursions are examined it will be noted that a slow rise of the balloon record usually accompanies the undulation in the electrocardiographic base line. This, then, is the first reproduction of simultaneous electrogastrograms and mechanogastrograms. However, there can be no

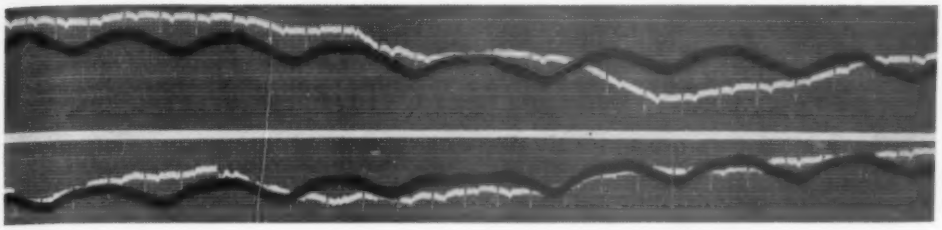

FIG. 1. Simultaneous electrogram by Lead III and mechanogram by stomach balloon. Note shift in base line of electrocardiogram accompanying balloon tracing. Note also minor respiratory and cyclic cardiac fluctuations.

identical parallelism because the electrocardiographic excursion by this method does not begin until the visible peristaltic wave has crossed the fundic portion and traverses the mid line, a fact previously noted. In other words, the peristaltic wave can be seen moving across the left hypochondrium to the right even without photographic confirmation, but the actual deflection in the electrocardiographic base line does not appear until the mid line has been crossed, probably because of the nature of the summation of the stresses. Furthermore, absolute parallelism of electro- and mechanograms by the balloon method is only exceptionally achieved because the mechanical method has a lag and for other reasons gives only a crude reproduction of stomach activity. First, the balloon is never large enough or in sufficient contact with the stomach wall to mirror the entire organ. Second, at a given moment, the balloon may lie in the pyloric portion and fail to reproduce fundic waves, particularly if the algebraic sum of contraction wave preceded by dilatation fails to alter intragastric and therefore balloon pressure. Third, even if the balloon lies in the path of the wave the algebraic sum of all effects on pressure may be zero. Fourth, pyloric waves are more effective than fundic ones. Fifth, the ordinary stomach balloon usually lies in the fundic portion. To obtain a more comprehensive picture of the entire stomach in action which usually has two or more waves passing at the same time, two or three separate balloons could be used lying in different portions of the stomach. However, even this method is not entirely accurate. The electrical stresses summate in a manner different from the mechanical changes. It is obvious that under certain circumstances, the electrical stresses may nullify each other in the direction of the lead in use and result in no change or shift in the electrical record. Nevertheless, enough is shown

to give objective evidence of mechanical muscular activity associated with electrical changes.

Study B. Direct leads were placed on the abdomen to approximate the positions of pyloric and cardiac ends of the stomach. The stomach balloon was connected to the Frank capsule as in the preceding record. (Figure 2.)

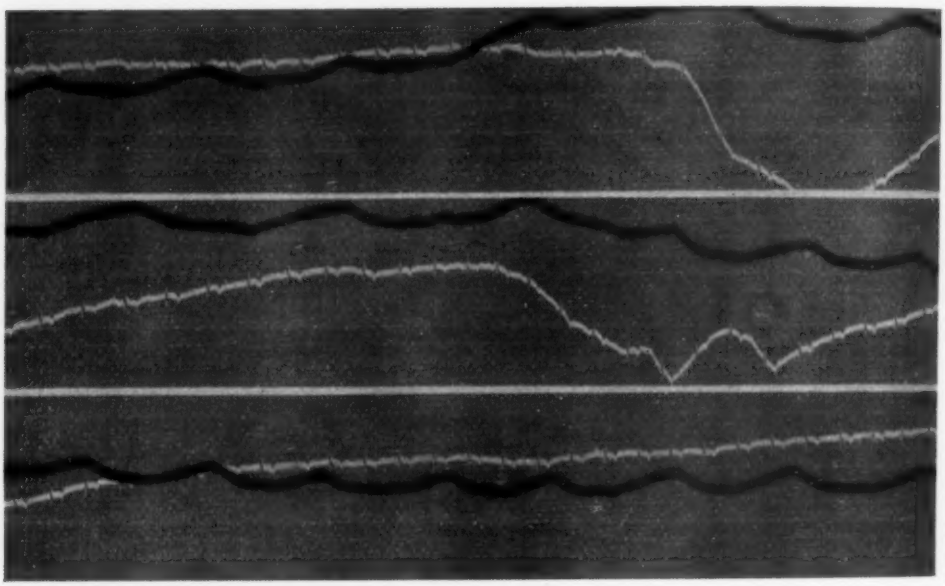

FIG. 2. Simultaneous gastric electrogram by direct abdominal leads and mechanogram by balloon. Note marked excursions of electrical and mechanical tracing and lack of absolute parallelism.

Comment. By this method the electrical undulations were extremely marked. Polarity was such that the electrical and mechanical records sometimes moved in opposite directions as the contractions enhanced the mechanogram deviations. The record submitted minimizes the electrical excursions because the string repeatedly moved off the camera slot and had to be returned. At one point the measurement indicated a 30 millivolt change. To answer the question whether the marked excursions might be artefacts due to the position of the abdominal wall and the change in position of the electrodes which were forced up during the marked peristaltic bulgings, the patient was instructed to vigorously distend and contract his abdomen by deep respirations. These measures and deep palpation of the epigastrium produced no significant effect. Therefore, it seems that gastric peristalsis alone produces a marked electrical wave which can be picked up when direct abdominal leads are employed. Furthermore, it was noted that the closer the left lead, i.e., the cardiac, was placed to the right, i.e., the pyloric, the greater the electrical excursions.

Study C. The typical Lead III was restored, but the mechanical deviation was recorded by fastening a tambour commonly employed to record the cardiac apex beat in the path of the peristaltic wave (a) left upper quadrant in the fundic region, (b) mid line and (c) in the region of the pylorus.

Comment. Although the observations correspond with those obtained by the preceding methods, namely, that electrical and mechanical deviations were demonstrated together, there was more difficulty because the nature of the peristaltic wave prevented accurate apposition of the tambour to the abdominal wall at all times.

Intestinal hyperperistalsis was observed in a girl with congenital hypertrophic dilatation of the colon (Hirschsprung's disease).

Case Report

R. M., a female of six and one-half years, was admitted to the Sarah Morris Hospital, service of Dr. Jesse R. Gerstley, October 18, 1934, for an acute dysentery which had affected three other members of the family after a meal of canned meat; and was discharged recovered from dysentery, November 5, 1934. Interest in connection with the present study lay in the fact that constipation had been present since the child was 14 days old. At this time she had no bowel movement for five days. At present she requires an enema every two or three days without which there is no evacuation. There has been loss of sphincter control at intervals since infancy. These involuntary movements are sometimes loose and associated with simultaneous urination. Further, there is frequent involuntary urination when the bowels are unusually constipated. (It should be stated here that atony of the bladder is commonly associated with atony of the colon and is usually overlooked in the history and examination.) It was also volunteered that the child had never been quite well and that her extremities had remained poorly developed while her abdomen became large and protuberant.

Physical examination revealed a small undernourished girl with thin arms and legs and an unusually large abdomen, slightly toxic and feverish. Aside from the specific illness for which she was admitted, it was noted that a relatively long torso gave a peculiar appearance. There were large peristaltic waves passing from right to left across the abdomen and also down the left side of the abdomen from above, following the course of the colon. Tympanites was present, and the bladder was distended. An opaque enema revealed a localized segment of dilated distal colon. The enema filled the dilated loop and extended backward to fill a tremendously dilated colon throughout. After 24 hours practically the entire enema was still present within the colon.

Study D. Lead III which was used in other portions of this report was employed for the electrical record. A tambour was placed on the abdomen connected for photographic registration of mechanical effects as described above. (Figure 3).

Comment. The wide deviations of the band which again reproduces the mechanical record indicates the violence of the intestinal peristalsis. This is further evidenced by the tracing leaving the limits of the camera in several places. Equally conspicuous is the marked rise and fall in the electrocardiographic base line associated with the greatest activity of peri-

stalsis. In the portion of the record here illustrated it is mere chance that the electrical and mechanical excursions are in the same direction because a wave in another segment of colon may be associated with an electrical wave in the opposite direction depending on the interference and direction of the interference of the electrical axis. A review of results in a previous study

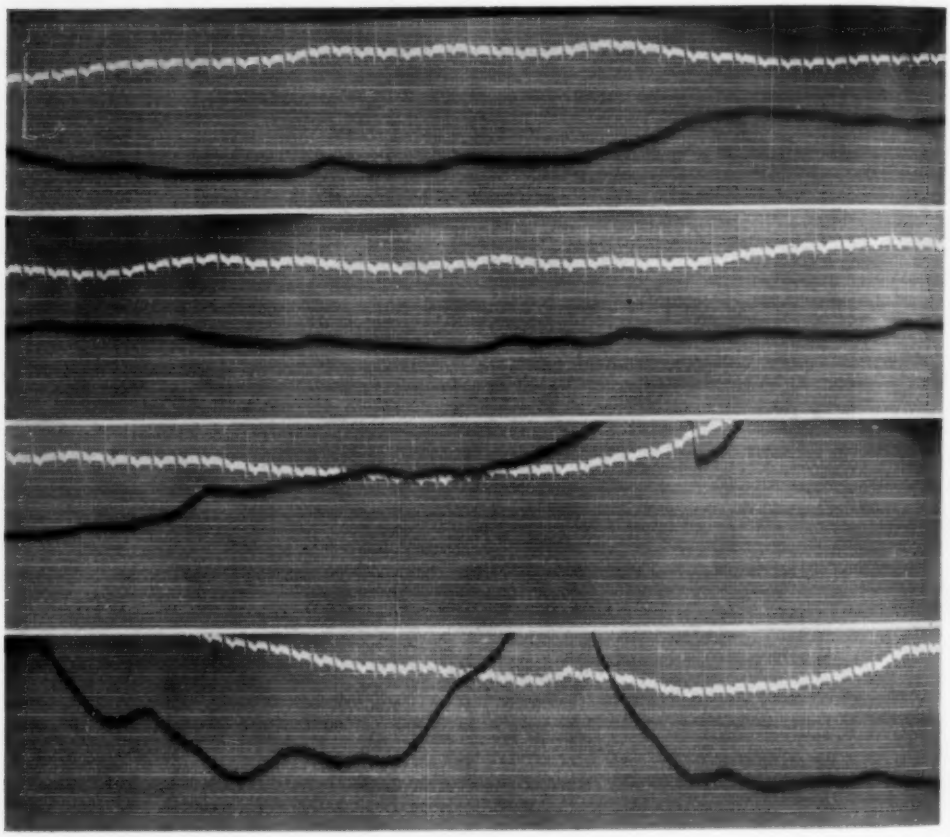

FIG. 3. Simultaneous electrogram by Lead III and intestinal mechanogram by tambour. Note degree and direction of fluctuations.

in intestinal hyperperistalsis in a two year old child with Hirschsprung's disease and in a 60 year old man with borborygmi will recall that there is no regularity in curves because the intestinal wave is a variable at any given moment in direction, intensity and location. These variable factors must affect the electrocardiogram irregularly. The waves in the present subject were of marked intensity, and the algebraic sum of the peristaltic effects, checked visually, is illustrated in the reproduction. It is obvious that the tambour method is limited by the fact that it can only reproduce the mechanical changes of one small area, but it is useful in objectively denoting the mechanical effect of peristalsis and is an objective substitute for mere visual evidence.

Summary

1. Simultaneous mechanical and electrical registration of gastric hyperperistalsis is recorded for the first time in the intact human subject upon the electrocardiographic film.

a. The electrogastrogram and the mechanogastrogram resemble each other in form and contour because there is fixed polarity in gastric peristalsis.

b. The exact reflection of the electrical action current in gastric peristalsis cannot be mirrored by the balloon or tambour method because of the limitations of this method of reproducing the mechanical factor in contraction.

i. The algebraic total of contraction in electrical terms in its effect on the electrocardiogram is recorded.

ii. The algebraic total of stomach activity by changes in intragastric pressure or pressure within balloon or tambour is at best but crudely reproduced.

2. Simultaneous electrical and mechanical registration of intestinal hyperperistalsis is recorded.

3. This study accomplishes its purpose which was to confirm the author's previous observations by submitting objective evidence of simultaneous gastric and intestinal hyperperistalsis accompanying disturbances of the electrocardiogram coincident with visible peristalsis.

4. An exact picture may be possible by simultaneous cinematographic roentgenographic reproduction of visible peristalsis using a double coated barium treated balloon and electrocardiographic records run on film at equal speeds.

5. This study confirms the fact previously established that the movements of the base line of the electrocardiogram are the electrical evidence of hyperperistalsis and can properly be called hyperperistalt-electrograms.

6. Indirect electrical leads are adequate and may serve a useful function in the study of peristalsis.

I wish to acknowledge indebtedness to Dr. Heinrich Necheles of the Department of Gastro-Intestinal Physiology for his suggestions and assistance and to Dr. Louis N. Katz, Director of Cardio-Vascular Research, for advice on methods of registration and for his valuable suggestions in the preparation of this report.

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THE VALUE OF THE SEDIMENTATION TEST AS A DIAGNOSTIC AID *

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In 1918, Fåhraeus [1] called attention to the fact that there was an increase in the sedimentation rate of red blood cells in the citrated blood of pregnant women. This was immediately hailed as a new test for pregnancy. However, it was soon discarded, as it was found to be unreliable, until after the third month of pregnancy.

Fåhraeus was not the first to make this interesting observation. Galen, as early as the year 200, pointed out that if blood were allowed to stand in a tube, a white line would form at the top of the blood. While he did not recognize this white line as coagulated plasma, he did regard it as pathological, and referred to the phenomenon as the "Crusta Phlogistica." In 1791, John Hunter noted that the erythrocytes of the blood settled more rapidly in inflammatory conditions than they did in normal blood. Further observations were made by Nasse in 1836, Davy in 1839, Müller in 1844, and Biernacki in 1894.[2]

The test was then forgotten until the work of Fåhraeus. In 1920, Linzenmeier [3] called attention to its usefulness in the diagnosis of pyosalpinx. Friedlander in 1924, Polak in 1926, and Baer and Reis, in the same year, called further attention to its use in gynecology and obstetrics, while Wehrbein, in 1928, stressed its importance in urology.

Technic

Unfortunately, there are three different methods of performing this test, and each in turn has different modifications, made by various investigators. The first method is that of Fåhraeus and Westergren. The underlying principle in this consists of measuring the distance through which the red blood cells fall in one hour; and the results are recorded in millimeters. The second is the Linzenmeier [3] method, in which a record is made of the time in minutes necessary for cells to settle a given distance of 18 millimeters in a column of blood 50 millimeters high. The third is the graphic method of Cutler,[4] in which the use of a graph is especially valuable, as it shows any sudden change in velocity.

Greisheimer [5] and his associates have pointed out that the average sedimentation rate in one hour for "normal" subjects appears to be reasonably concordant for the three methods, despite the wide difference in the width of the tubes, the length of the fluid column, and the anti-coagulant concentration.

Wintrobe and Landsberg [6] have emphasized the necessity of a standard test and pointed out many possible sources of error in performing the test.

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The most important are the following: The effect of the anti-coagulant; the influence of the bore and length of the tube; the influence of the inclination of the tube; the effect of the room temperature; the changes in the suspension stability of blood, as influenced by delay, in carrying out the test.

In our work, the Schiller modification of the Fåhraeus-Westergren method was used. It has several advantages, the most important being that the technic is simple, the time required for observation is only one hour, the recording of only one reading is necessary, and the blood is obtained from the finger and not the vein.

A capillary tube 138 millimeters long and 1 millimeter in calibre is used. There are two marks on the tube, the first being 13 millimeters, and the second 63 millimeters from the tip. After preparing the patient's finger in the usual manner, and making a quick puncture, a 5 per cent solution of sodium citrate is drawn up to the first mark, and the patient's blood is immediately drawn to the second mark, great care being exercised to prevent the formation of air bubbles. The tube, which contains 0.4 c. c. of citrate and 1.6 c. c. of blood, is gently tilted 20 times to allow the solutions to mix. The tip of the tube is then plugged with a tiny piece of soap and carefully placed vertically in an especially constructed rack, which has clamps to hold the tube very firmly. After exactly one hour, the amount of clear fluid at the top of the tube is read and recorded in millimeters. The normal rate for males is 2 to 8 millimeters, the average being 4 millimeters, while the normal for females is 3 to 10 millimeters, with an average rate of 6 millimeters. The normal rates for infants, children and senile individuals, is slightly greater, while the same is true of menstruating women.

Theory

Various factors influence the speed with which erythrocytes settle but, as yet, the exact mechanism of the sedimentation test is not known. Numerous explanations have been advanced. Fåhraeus[1] believes that increased sedimentation is produced by an alteration in the electrical charge of the blood corpuscles, causing a loss of their repelling force, and thereby bringing about their agglutination and more rapid sedimentation. Reyner[7] holds that a difference in surface tension of blood plasma is responsible for the phenomenon. Hunt[8] states that whatever is responsible for the increased sedimentation is contained in the blood plasma, and that it is most likely an increase in the fibrinogen. According to Snappier,[9] the two chief factors influencing the rate of the fall are the concentration of fibrinogen and serum globulin, with hydration or degree of anemia acting as subsidiary factors. Hoverson and Petersen[10] regard the variations in the individual rates as dependent largely on environmental and meteorologic conditions. According to Gram,[11] the sedimentation rate depends on: (a) the cell volume percentage; (b) the fibrin percentage in the plasma, and (c) the temperature. On the other hand, Bortree[12] states that the relative speed of sedimentation

of erythrocytes is dependent upon the colloidal chemistry of the blood and chiefly upon the fibrinogen-globulin ratio. Koelsche [13] thinks the rate of sedimentation is directly proportional to the content of fibrin in the plasma. He points out that the blood of an anemic patient has a rapid sedimentation rate, notwithstanding its normal content of fibrin. An increase in viscosity of the blood inhibits sedimentation. Rubin and Smith [14] conclude that, in general, the lower the hemoglobin content of the blood, the more frequently is increased sedimentation obtained. They believe that the volume of red blood cells exerts an important influence on the sedimentation rate, under all conditions, and that possibly physiologic changes in sedimentation are also influenced, to a great extent, by the erythrocyte factor. Thus, the lower cell volume percentage found in women would explain the greater sedimentation reactions that they give in comparison to men. Among the various explanations of the varying rate of sedimentation of erythrocytes, Banyai and Anderson [15] feel that the most plausible are: (a) an increase in the fibrinogen content of the blood plasma and (b) changes in the number and size of the erythrocytes. Toxin production involves a breaking down of tissue proteins, and subsequently, the products of disintegrated tissue proteins will stimulate fibrinogen formation. As Cutler [16] points out, there is constantly a process of tissue destruction, accompanied by a similar amount of tissue repair. Should the amount of tissue destruction pass beyond the normal, then the stability of the blood is seriously disturbed and the red blood cells settle out quickly from the plasma, the rapidity of the settling of the red blood cells being in direct proportion to the severity of the disease.

We believe the sedimentation rate depends on the presence of a foreign protein in the circulation. In pregnancy, this is the protein of fetal catabolism; in infection, it is the protein of bacteria, and in malignancy or coronary occlusion, it is the protein of necrotic tissue.

Uses

As stated above, this test was first devised as a test for pregnancy. However, more recently, it has received recognition as a useful diagnostic adjunct in other branches of medicine. Westergren [17] claims that it not only has diagnostic value, but also furnishes information as to prognosis, as well as indications for therapy.

Cutler [18] presents the amazing statistics of 5,000 patients, on whom sedimentation tests were made. Of this entire group, there were only five patients on whom a normal rate was obtained, in the presence of active disease. Yates and Davidow [19] made 6,000 determinations on 1,700 patients and found the accuracy of the sedimentation test to be 91.4 per cent.

In our own work, we performed 488 sedimentation tests on 395 patients. Of 283 determinations that should have given normal sedimentation rates, only 11 had rates that were over the normal limit. Of the remaining 205 determinations which were expected to be abnormally high, there was not one single case that gave a rate of less than 15 millimeters.

Gallagher [20] presented figures on 685 normal school boys and concluded that the test produced most valuable results. In his group there were many patients with mumps and the "common cold." These gave normal rates, showing how little the sedimentation rate is affected by minor infections, of short duration.

The sedimentation test has been used very extensively in the field of gynecology. Grodinsky [2] called attention to an increased rate in pyelitis, pyelonephritis, pyonephrosis and perinephric abscess. He found that ureteral colic, and other urological conditions, without associated infection, gave a normal rate, and emphasized the importance of this in the differential diagnosis of pain in the lower right quadrant. He further noted that acute appendicitis without rupture had a relatively low rate, while subacute and chronic appendicitis gave even a lower figure. Polak and Tollefson [21] cite 1,660 readings on 650 gynecological patients. They concluded that rapid sedimentation indicated infection, when the readings in pregnancy and the puerperium had been excluded. In the presence of a high rate, these authors never operate on a patient, unless there be inflammatory process too active to permit conservative procedure. Furthermore, the test is used as an indicator by these investigators, as to the proper time to discharge the patient from the hospital. The individual is not released, until the rate returns to normal, excluding, of course, all other sources of infection. Polak and Tollefson use as their dictum, "The sedimentation test never lies." Ward [22] used the test in 1,140 cases and reached the same conclusion. Friedlander,[23] after testing 1,500 patients, felt that the test was extremely valuable in determining the "safe period" for operation. Schattenberg [24] after 1,100 tests, Rubin,[25] Nicholson,[26] and Stimson [27] are all in accord in this respect.

Smith, Harper and Watson [28] in their report of 19 cases of acute salpingitis and 38 cases of acute appendicitis, came to the conclusion that the sedimentation test is of some value as a differential point between these two conditions. Nicholson [26] was of the same opinion.

Mathieu, Trotman and Haskins [29] performed 2,100 tests on 1,145 patients. Of these, 220 tests were on healthy women. They found that in abortions without infection, the sedimentation rate returned to normal, 15 days after curettage. They further noted that in eight cases of ruptured ectopic pregnancy, the sedimentation rate was increased, but in no case was it as high as in acute or subacute salpingitis. The difference, however, was not sufficient to regard this as a differential test between the two conditions. They found normal rates in 40 cases of trichomonas vaginalis vaginitis, 13 cases of Fröhlich's syndrome, and 80 cases of cystocele, rectocele, retroversion and prolapse of the uterus; but the rate was definitely elevated in 23 cases of infection of Skene's or Bartholin's glands.

Lesser and Goldberger [30] reported 2,000 cases of all conditions with 3,000 readings. They felt that it was even possible to differentiate acute appendicitis from acute rheumatic fever with abdominal symptoms, by

means of this test. The latter had a very high, while the former had an absolutely normal reading. They included 75 cases of acute appendicitis made up of catarrhal, gangrenous and suppurative, and observed that uniformly the sedimentation rate was normal, regardless of the pathologic lesion noted. On the other hand, all other types of acute surgical conditions in the abdomen, including ruptured appendix, gave an elevated reading.

Rubin [25] concluded that in surgery, the sedimentation rate is a more reliable indication of the condition of the patient than the temperature chart. Nystrom and Geisheimer,[31] in reporting 57 gynecological cases, and Smith, Harper and Watson [28] feel that the sedimentation test gives more valuable information than the temperature chart or the white blood count.

On the other hand, Simmich,[32] after an observation of 150 gynecological patients, of whom 132 had laparotomies, stated that the sedimentation rate was not a reliable guide in the determination of the safe operative time, and Williams [33] concluded after his study that the temperature curve and the study of the leukocytes remain as more stable indices for diagnosis and prognosis. Peterman and Seeger,[34] in reporting 150 cases in children, were of the same opinion.

From our studies, we are inclined to disagree with the views of this latter group. We observed 73 cases, which were normal in every respect and which had a normal sedimentation time but in whom the white blood count was over 10,000 in each case. Of these 73 cases, 19 had white counts of over 13,000 and in seven of these, the white blood count was over 16,000.

In 70 of these cases, the differential count was normal. One of these cases was especially interesting. The patient, a man of 42 years of age, had evidence of myocardial damage. He continued to have fever and leukocytosis for several months, during which time the sedimentation rate remained absolutely normal. Very careful investigation revealed no evidence of infection, and after a time the fever and leukocytosis disappeared. (Table 1.)

TABLE I

The laboratory records of a patient showing fever and leukocytosis together with a normal sedimentation rate

Date	Hb.	R. B. C.	Sed. Rate	W. B. C.	Diff.	Temp.
3/11/35	90	4,560,000	8	12,300	Normal	99.4
3/20/35	88	4,620,000	7	11,900	Normal	99.1
4/8/35	88	4,640,000	8	10,150	Normal	99.0
4/24/35	90	4,720,000	6	12,900	Normal	99.2
5/5/35	87	4,670,000	8	17,400	Normal	98.4
5/20/35	89	4,700,000	8	16,200	Normal	99.0
6/5/35	86	4,680,000	7	11,950	Normal	99.1
6/24/35	88	4,800,000	8	10,250	Normal	99.1
7/1/35	89	4,840,000	6	11,200	Normal	99.2
8/13/35	90	4,750,000	3	8,600	Normal	99.0
9/3/35	87	4,680,000	5	13,700	Normal	98.4
9/13/35	89	4,320,000	8	17,200	Normal	99.0

Malignant growths, if extensive, usually give a high sedimentation rate,

while a slow growing benign tumor without necrosis gives a normal rate. However, after irradiation of any tumor, the rate of sedimentation increases, probably due to decomposition of the tumor, with a resultant increased amount of foreign protein in the blood. According to Schiller,[35] if a malignant growth be removed operatively, the sedimentation rate should return to normal within six weeks, if complete removal was obtained. If the rate returns to normal, and remains normal at least six months, one may give a guardedly favorable prognosis. If the rate becomes abnormal within this time, it is suggestive of local recurrence of the growth or metastasis. In one of our cases, the patient, a woman of 62, had what appeared to be a typical fibroid, about the size of a grape fruit. The hemoglobin was 85 per cent, r. b. c. 4,730,000, w. b. c. 6,750, and the differential count was normal. The sedimentation rate, however, instead of being the normal as in a simple fibroid, was 32. The uterus when removed appeared grossly to be a fibroid, but on closer microscopical examination, malignant degeneration was found to have occurred at the central part of the tumor. Two months after the operation, the sedimentation rate was 8. There were seven other cases of malignancy in our group, with 19 determinations, all of which were over 28 millimeters. Four of these were carcinoma of the stomach, and in each the hemoglobin was over 65 per cent. It is interesting to note that, on the other hand, there were 11 cases of definite duodenal ulcers with a total of 28 determinations, and in not one did the readings go over 6 millimeters. Four of the cases had hemoglobin lower than 65 per cent.

One of the greatest uses for this test is in determining the degree of certain infections. If the infection be in the active state, the rate will be high, while if the infection be in the arrested state or state of repair, the rate will be low. It has been especially useful in infectious arthritis and tuberculosis. Oppel, Meyers and Keefer [36] studied 107 patients with various forms of arthritis and 103 with a miscellany of diseases, as a control group. They found a great variation in the sedimentation rate in different types of arthritis, the most rapid rate being in acute rheumatic fever, rheumatoid and gonorrheal arthritis. In our series, there were 23 readings made on nine patients with acute arthritis. In each the rate was elevated, ranging from 26 millimeters to 48 millimeters. An interesting observation is the uniformity of this test over a long period of time, as compared with the marked variability of the white blood count. (Table 2.)

TABLE II

A case of acute arthritis illustrating the relative constancy of the sedimentation rate

Date	Hb.	R. B. C.	Sed.	W. B. C.	Polys.
10/15/34	85	4,340,000	38	10,600	74%
11 15/34	80	4,130,000	33	13,350	76%
12/14/34	80	4,000,000	32	12,300	73%
1/15/35	82	4,730,000	36	10,000	74%
2/23/35	82	4,600,000	34	12,400	71%
3/23/35	86	4,920,000	36	7,600	73%
4/18/35	80	4,250,000	35	10,850	70%

Furthermore, as the patient improves, there is a tendency for the sedimentation rate to decrease. (Table 3.)

TABLE III

Case illustrating parallelism of clinical improvement and decrease of sedimentation rate

Date	Hb.	R. B. C.	Sed.	W. B. C.	Differential	General Condition
7/24/35	91	4,480,000	39	9,700	Normal	Bed-ridden. Painful swollen feet.
9/ 8/35	90	4,670,000	24	7,200	Normal	Bed-ridden. Feet not so red. Ambulatory. Feet not so red or painful.
9/25/35	90	4,600,000	8	9,950	Normal	Feet much better.
10/10/35	92	4,650,000	5	10,100	Normal	Condition greatly improved.

This is not only true in arthritis, but also in other infections. Table 4 represents the findings in a patient of 14, with acute endocarditis, who showed simultaneous improvement in his clinical condition and in the sedimentation rate.

TABLE IV

Case of rheumatic carditis showing clinical improvement and decreasing sedimentation rate

Date	Hb.	R. B. C.	Sed.	W. B. C.	Differential	General Condition
8/13/35	83	4,430,000	36	7,300	Normal	Bed-ridden; dyspnea; pain.
9/ 3/35	85	4,460,000	25	6,000	Normal	Bed-ridden. Slower pulse.
9/16/35	82	4,310,000	14	11,650	Normal	Bed. Less dyspnea.
10/ 1/35	83	4,300,000	7	6,850	Normal	Sitting up. No fever or pain.
10/15/35	86	4,510,000	5	10,300	Normal	Ambulatory, much improved.

In tuberculosis infections the sedimentation rate is high in the presence of activity and normal in the arrested stage. The value of this test in tuberculosis has been widely recognized, especially in the European clinics. In certain Austrian tuberculosis sanatoria, a sedimentation test is made routinely three times a week on each patient. The usefulness of the test in this field is emphasized by Grafe [37] who reported 500 cases, Rubin,[38] Van Antwerp,[39] Cutler and Cohen,[40] Banyai and Anderson,[15] Ringer [41] and others. Cutler and Cohen believe it to be 94 per cent accurate in tuberculosis. They point out that a higher reading is obtained if the patient is unduly excited. Banyai and Anderson, in 2,000 cases, found a normal sedimentation time in 128 cases with signs of activity, an error of 7.35 per cent. They feel that the test's greatest value is in its use as an objective measure of the course of the disease. It serves as a sensitive indicator of complications or the development of new foci, and as a criterion of results obtained

by a regimen or a specific treatment. New foci in lung tissue are sometimes not suspected, and complications like intestinal or renal tuberculosis are often not detected until an increase in the sedimentation rate has led to a careful search. It offers an approximate gauge of the extent of improvement when physical or roentgen examination may be of little value. Ringer pointed out that a rise in the rate in a tuberculous patient may precede hemoptysis. His two years experience with the test has convinced him that the test is one of real value. It reinforces physical, radiological and symptomatic evidence, and frequently presages oncoming trouble. He emphasized the fact that no tuberculous patient should be discharged until the sedimentation rate is normal. In our small series, we had six arrested cases of tuberculosis, none of which had a sedimentation time of over 7 millimeters, and one active case with a rate of 39.

In addition to these, there are other uses for this test as mentioned by Sivinsky,[42] Tulipan and Director. Recently attention has been drawn to its usefulness in cases of coronary occlusion. In this condition the rate becomes elevated a few hours after the onset of the attack. The increase is probably due to the absorption of necrotic tissue from the produced myocardial infarct. After reaching its peak, the rate gradually diminishes. The duration of this period of elevated rate may serve as a guide in determining how long the patient should be kept at rest. It may therefore prove useful not only as a diagnostic measure, but also as a measure of the healing of the infarct. (Table 5.)

TABLE V

The sedimentation rate following coronary thrombosis

Patient	Sed. Rate prior to Attack	1st Wk. of Attack	3rd Wk. of Attack	4th Wk. of Attack	5th Wk. of Attack	6th Wk. of Attack	12 Wks. after Attack
E. W. E.	6	46	35	25	10	7	5
C. W. G.	7	45	42	20	7	5	4
T. H.	—	40	32	24	16	8	—
H. L. M.	4	58	44	30	20	7	6
C. S.	—	45	36	21	15	8	—
A. G.	—	48	—	—	—	—	—

SUMMARY AND CONCLUSIONS

1. The sedimentation test is a relatively simple laboratory procedure which is now soundly established as a valuable addition to our diagnostic armamentarium.

2. The sedimentation test is not a specific diagnostic test for any one condition, but the presence or absence of an increased sedimentation rate may have great value in differential diagnosis.

3. The comparison of repeated sedimentation tests is particularly useful in estimating the progress of disease. The test is now widely employed

in this manner in gynecological diseases, in tuberculosis, in rheumatic infections, in malignant growths and recently in coronary occlusion.

4. The results obtained in 488 sedimentation tests on 395 patients were found confirmatory of the reliability of the test. Charts furnishing examples of the utility of the test are included. The results obtained with the test in six cases of coronary occlusion are tabulated.

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CLINICAL EXPERIENCES WITH REDUCED DOSES OF THEVETIN ORALLY ADMINISTERED *

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Clinical studies of the action of thevetin [1, 2] have amply confirmed the pharmacologic results of Chen and Chen [3, 4] and established its reliable digitalis-like effect in man. The pulse is slowed, evidences of decompensation are alleviated, diuresis ensues and characteristic electrocardiographic changes occur when thevetin is given either by the oral or the parenteral route. Its untoward by-effects also parallel those of digitalis with a singular deviation in the gastrointestinal action. Here intestinal effects (cramps and diarrhea) in the main replace the common gastric upsets (anorexia, nausea and vomiting) incident to digitalis intoxication.

The galenical preparations of the defatted be-still nuts, which are the source of the glucoside, thevetin, gave practically constant evidences of gastrointestinal irritation.[1] Indeed, this action was so serious as to preclude their further clinical trial. On the other hand the glucoside, thevetin, parenterally or orally administered, proved a distinct improvement over the galenical products in this respect.[1, 2] Even with thevetin, however, 16 of 40 patients with cardiac decompensation showed some gastrointestinal effects.[2] Of this group 11 patients after a period of rest were able to resume the use of the drug without a recurrence of abdominal symptoms. The failure of concurrently administered belladonna to control the cramps and diarrhea caused by thevetin argues against Chopra and Mukerjee's suggestion that these phenomena are due to peripheral vagal action.[5] Furthermore, atropinized intestinal strips from the rabbit show vigorous contraction upon the application of thevetin.[2]

A re-survey of the situation [2] evolved certain illuminating circumstances. The minimal emetic dose of thevetin is equivalent to 35 per cent of the cat unit as compared with 50 per cent for ouabain. Intestinal strips of rabbits are stimulated by minimal concentrations of thevetin and ouabain in the ratio of 3 1/3 : 1 as compared with the ratio of cat unit values of 7 : 1. In other words one may expect gastric and intestinal effects much more promptly in relation to the cat unit with thevetin than with ouabain. Clearly, too, the intestinal action of thevetin may be expected to precede its effect on gastric function.

On the other hand a maximal bradycardia is induced with 30 per cent of the cat unit of thevetin as compared with 58 per cent for ouabain. Accordingly it seemed reasonable to anticipate an optimal clinical advantage with one half the cat unit dosage of thevetin as compared with ouabain. Since

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TABLE I

No.	Age	Sex	Wt.	Prior Digitalis	Type Heart Dis. / Functional Cap.	Thevetin Dosage	Interval Days	Initial Effect: Circulatory Subjective	Initial Effect: Circulatory Objective	Initial Effect: Gastric	Initial Effect: Intestinal	Further Thevetin	Subsequent Effect: Circulatory Subjective	Subsequent Effect: Circulatory Objective	Subsequent Effect: Gastric	Subsequent Effect: Intestinal	Comment	Symbolic Value of Thevetin Therapy *
1	49	M	186	Tr. M. XV t.i.d. 12/28/35 to 1/9/36 Maintenance M. V t.i.d.	Rheumatic; Grade III	M. X t.i.d.	3	0	0	Nausea, Vomiting	Diarrhea	M. V t.i.d. (3 days)	0	0	0	Involuntary diarrhea	After 3 days of thevetin pulmonary infarction occurred. Expired 11th hospital day. P.M. Mural thrombosis left auricular appendage. Pulm. infarcts on left with CPC lungs, liver and spleen.	−
2	56	M	240	Tr. M. XV t.i.d. Indefinite. M. XV t.i.d. on 1st day of admission	Hypertensive; Grade III	M. XV t.i.d.	5	Improved; less dyspnea	Vagal effect; Diuresis; Edema reduced	0	0	M. VIII t.i.d., 3 days; M. V t.i.d., 5 days	Improved	Maintained vagal effect	Anorexia nausea, 3 days; better for 5 days	Pain left abdomen. Tendency looseness bowels (1 day). No diarrhea	Improvement marked with diuresis. Theocin begun on 7th hosp. day. Nausea followed. Theocin discontinued after 3 days. Nausea disappeared 2 days later. Signed his own release on 22nd hospital day.	+
3	62	M	142	0	Arteriosclerotic; Grade IIB	M. X t.i.d.	6	0	Vagal effect	0	0	M. V t.i.d. 1 day	0	Pulse maintained at slower rate	0	0	Patient severe asthmatic, which was primary condition.	+
4	50	F	106	0	Thyrotoxic; Grade IIB	M. XV t.i.d.	3	0	Vagal effect marked	0	0	M. XV t.i.d. 3 days; M. V t.i.d. 6 days; M. XV t.i.d. 4 days	0	Pulse was maintained at a slower rate	Nausea	Cramps, Diarrhea	This patient had thyroidectomy. While thevetin slowed the pulse rate it caused diarrhea, nausea and cramps. Finally was discontinued and patient placed on digitalis.	− +
5	45	M	167	0	Hypertensive; Grade III	M. V t.i.d. 1 day; M. X t.i.d.	8	Improved	Early vagal effect. Diuresis. Decreased cyanosis	0	0	M. V t.i.d. 1 day	Continued improvement		0	0	Patient also received theophyldine gr. iss t.i.d. and ammon. chloride. Later theocin gr. X given t.i.d. for 3 days. Early vagal effect not maintained proportionally to general advantage.	+

* Symbolic Value of Thevetin Therapy:
Circulatory advantage marked, +
Circulatory advantage less marked and accompanied by minor gastrointestinal effects, ±
Pronounced gastrointestinal effects and less marked circulatory response, ∓
Predominant gastrointestinal effects and minor circulatory response, −

TABLE I—*Continued*

Predominant gastrointestinal effects and minor circulatory response, —

TABLE I—*Continued*

No.	Age	Sex	Wt.	Prior Digitalis	Type Heart Dis. / Functional Cap.	Thevetin Dosage	Interval Days	Initial Effect				Further Thevetin	Subsequent Effect				Comment	Symbolic Value of Thevetin Therapy *
								Circulatory		Gastric	Intestinal		Circulatory		Gastric	Intestinal		
								Subjective	Objective				Subjective	Objective				
6	61	M	165	M. X t.i.d. 5 wks. Digalen gr. iss t.i.d. 1 week	Arteriosclerotic; Grade III	M. XV t.i.d.	3	Improved	Diuresis. Vagal effect marked	0	0	M. XV t.i.d. 1 day; M. V t.i.d. 2 days; M. X t.i.d. 2 days; M. V t.i.d. 5 days	Cyanosis Dyspnea	Diuresis (slight)	Nausea Anorexia	Diarrhea; no cramps	In view of anorexia and loose stools thevetin was discontinued, although vagal effect was obvious. Placed on digalen. Symptoms of nausea, anorexia, diarrhea persisted. Patient expired 48 days following discontinuance of thevetin.	− +
7	32	M	177	0	Hypertensive; Grade III	M. X t.i.d.	8	Less dyspnea. Improved	Decrease in pulmonary congestion. Vagal effect marked	0	0	M. V t.i.d. 4 days; M. VIII t.i.d. for 14 days	Improved	Pulse maintained slower rate	Slight nausea. Anorexia	0	Developed a patch of bronchopneumonia on 35th hospital day. Recovery uneventful.	+
8	75	M	169	0	Arteriosclerotic; Grade III (Lymphocytic leukemia)	M. X t.i.d.	6	Improved	Vagal effect marked	0	0	M. X t.i.d. 7 days; M. V. t.i.d. 22 days	Improved	Pulse maintained at slower level	0	Diarrhea	Picture complicated by a chronic lymphatic leukemia for which he was given deep roentgen-ray therapy. Diarrhea controlled upon lowering dosage of thevetin.	+
9	51	M	?	Tr. M. XV t.i.d. for 1 month	Thyrotoxic; Grade III	M. XV t.i.d.	8	Improved	Pulse slowed; marked vagal action	0	0	M. V t.i.d. 15 days; M. VIII t.i.d. for 7 days	Improved	Pulse maintained at slower level	0	0	Auricular flutter with varying degrees of block began 8 days after use of thevetin. Thyroidectomy done following which no digitalis or thevetin was given. Signs of decompensation returned. Patient was placed on digitalis by reason of change in service.	+
10	55	M	?	0	Thyrotoxic; Grade III	M. XV t.i.d.	6	Improved	Pulse slowed; diuresis. Edema decreased	0	0	M. V t.i.d. 28 days	Improved	Dyspnea persisted	0	0	Theocin used following which there were cramps and diarrhea. Theocin stopped and cramps disappeared. On continued use of thevetin pt. became constipated. Pt. expired 5 days following removal of thyroid gland. ? Pulm. embolism.	+

TABLE I—*Continued*

No.	Age	Sex	Wt.	Prior Digitalis	Type Heart Dis. / Functional Cap.	Thevetin Dosage	Interval Days	Initial Effect: Circulatory: Subjective	Initial Effect: Circulatory: Objective	Initial Effect: Gastric	Initial Effect: Intestinal	Further Thevetin	Subsequent Effect: Circulatory: Subjective	Subsequent Effect: Circulatory: Objective	Subsequent Effect: Gastric	Subsequent Effect: Intestinal	Comment	Symbolic Value of Thevetin Therapy *
11	54	M	222	0	Arteriosclerotic; Grade IIB	M. XV t.i.d.	4	0	0	0	Cramps, Diarrhea	0	0	0	0	0	After 4 days of thevetin cramps and diarrhea developed. Placed on Tr. digitalis M. XXX t.i.d. Suddenly expired 2 days later. (Pulm. thrombosis.)	−
12	74	M	136	Tr. Digitalis 1 month. Amount ?	Arteriosclerotic; Grade IIB	M. V t.i.d.	6	Improved	Continued vagal effect	0	0	0	0	0	0	0	Patient had been fairly well digitalized before admission. He was kept on a maintenance dosage of thevetin.	+
13	41	M	168	On digitalis 4 months. Amt. ?	Rheumatic; Grade IIB	M. XV t.i.d.	5	Improved	Vagal effect	0	0	M. V t.i.d. 3 days; M. X t.i.d. 2 days; M. V t.i.d. 21 days	Improved	Pulse maintained at slower level	0	0	On thevetin M. V patient complained of constipation. Progressive improvement. Change to digitalis made "heart pound."	+
14	90	M	180	Tr. Dig. M. X t.i.d. for 2 days	Arteriosclerotic; Grade IIB	M. X t.i.d., 3d M. XV t.i.d. 2 days	5	0	Vagal effect	0	0	M. XV t.i.d. 2 days	Improved	Pulse maintained at slower level	0	Slight diarrhea	Thevetin discontinued after diarrhea appeared. Definite vagal effect. Continued to improve after thevetin was discontinued.	+ −
15	75	M	140	0	Arteriosclerotic; Grade III	M. XV Q.I.D. 4d; M. X t.i.d. 10 days	14	Improved. Less dyspnea	Vagal effect marked. Diuresis. Edema decreased	0	0	M. VIII t.i.d. 2 days	Improved	Pulse was maintained at slower level	0	0	Patient given a course of Theocin gr. X t.i.d. just prior to marked diuresis. Edema disappeared. Dyspnea less marked.	+
16	28	M	?	0	Rheumatic; Grade III	M. XV t.i.d.	5	Improved	Moderate vagal effect	0	0	M. X t.i.d. 10 days	Dyspnea Cyanosis	Cheyne-Stokes respiration	0	0	Picture complicated by chronic alcoholism and thyrotoxicosis. Pt. expired with broncho-pneumonia.	−
17	49	M	?	0	Hypertensive; Grade III	M. XV t.i.d.	5	Improved	Vagal effect	0	0	M. X t.i.d. 5 days; M. V t.i.d. 7 days	Improved	Diuresis. Pulse at slower level	0	0	Circulatory balance was restored. Improvement was progressive and not attended by any complication.	+
18	65	M	?	0	Arteriosclerotic; Grade III	M. X t.i.d.	10	Improved. Dyspnea less	Vagal effect, diuresis. Decrease cyanosis	0	0	M. V t.i.d. 4 days	Improved	Pulse maintained at slower level	0	0	Picture complicated by Laennec's cirrhosis. Patient also given diuretics, ammonium chloride gr. XXX t.i.d. Abdominal paracenteses done.	+

TABLE I—*Continued*

TABLE I—*Continued*

No.	Age	Sex	Wt.	Prior Digitalis	Type Heart Dis. / Functional Cap.	Thevetin Dosage	Interval Days	Initial Effect: Circulatory Subjective	Initial Effect: Circulatory Objective	Initial Effect: Gastric	Initial Effect: Intestinal	Further Thevetin	Subsequent Effect: Circulatory Subjective	Subsequent Effect: Circulatory Objective	Subsequent Effect: Gastric	Subsequent Effect: Intestinal	Comment	Symbolic Value of Thevetin Therapy *
19	66	M	186	0	Arteriosclerotic; Grade III	M. XV t.i.d.	7	Improved. Less dyspnea	Vagal effect marked. Edema decreased	0	0	M. V t.i.d. 20 days	Improved	Pulse maintained at slower level. Better water balance	0	0	Improvement in circulation was continuous and maintained.	+
20	42	F	91	Tr. Digitalis M. X t.i.d. 16 days	Hypertensive; Grade III	M. X t.i.d.	3	0	Moderate vagal effect	Nausea	Diarrhea	M. V t.i.d after 12 days	0	0	0	0	Patient was started on Tr. Digitalis. Because condition did not improve changed to thevetin. Edema and congestion at bases persisted as well as gallop rhythm. Patient expired.	−
21	78	M	123	?	Arteriosclerotic; Grade IIB–III (Lymphocytic leukemia)	M. V t.i.d. 1 day; M. XV t.i.d.	4	Improved	Vagal effect. Diuresis	0	0	M. V t.i.d. 15 days	Improved	Pulse maintained at slower level	0	0	Patient received eight 25 r. units deep roentgen-ray therapy for leukemia.	+
22	59	M	180	Quinidine intermittently for 3 years	Arteriosclerotic; Grade III	M. XV t.i.d.	17	Improved	Vagal effect	0	0	0	Improved	Pulse maintained at slower level	0	0	This patient had an auricular fibrillation which had been treated with quinidine (amount not known) for 3 years. Precordial pain was fairly severe. Precordial pain was relieved for 1 week before discharge.	+
23	68	M	210	Digitalis. Amount ?	Arteriosclerotic; Grade III	M. X t.i.d.	2	Improved	Vagal effect. Diuresis	0	0	M. V t.i.d. 3 days	Improved	Continued vagal effect	0	0	Patient had been digitalized in Jan. 1936, 4 months before present admission. Thephyldine given with thevetin.	+
24	60	M	172	Digitalis ? Tr. Dig. M. XX t.i.d., first day	Hypertensive; Grade III	M. X t.i.d. 1 day; M. V t.i.d.	20	Improved. Less dyspnea and orthopnea	Vagal effect, diuresis. Edema decreased	0	0	0	Improved	Continued vagal effect	0	0	Improvement in circulatory condition was progressive. Ammonium chloride and Mercupurin used with resulting profound diuresis. Abdominal and thoracic paracenteses done.	+
25	68	M	192	0	Hypertensive; Grade III	M. X t.i.d.	8	Improved. Less dyspnea	Vagal effect. Edema decreased	0	0	M. V t.i.d. 8 days	Improved	Pulse maintained at slower level	0	0	Advantage maintained.	+

the earlier results indicated the appearance of a digitalis-like action from thevetin before theoretical tolerance on the body weight basis, such a readjustment of dosage seemed justified. At the same time the suggested reduced doses of 1 cat unit, three times a day, with a maintenance dose of 1/3 cat unit, three times a day, (as a maximum), offered the further prospect of an evaluation of the posssible effect of such a reduction of dosage upon the incidence of untoward gastrointestinal symptoms.

A group of 25 patients with cardiac decompensation was subjected to this revised program of reduced thevetin dosage. In table 1 are listed their several diagnoses and the pertinent clinical data, particularly relating to therapy, and the results therefrom.

Turning to the results of treatment, under " Symbolic Value of Thevetin Therapy," there will be found a rough assessment of therapeutic response.

TABLE II
Initial Effect of Thevetin

	Clinical Observations	Total Cases	Case Numbers
Circulatory Advantage	Subjective, only	0	
	Objective, only	3	3, 4, 14
	Both, combined	19	2, 5, 6, 7, 8, 9, 10, 12, 13, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25
Adverse Action	Gastric symptoms, only (anorexia, nausea, vomiting)	0	
	Intestinal symptoms, only (cramps, diarrhea)	1	11
	Both gastric and intestinal symptoms	2	1, 20

Obviously 18 patients responded favorably to the alcohol solution of thevetin given by mouth and in one further patient (case 14) there was a good result with but slight diarrhea. In two patients (cases 4 and 6) the circulatory advantage did not compensate for the adverse gastrointestinal symptoms. Finally in three patients (cases 1, 11 and 20) the severity of the gastrointestinal disturbance seriously outweighed the action upon the circulation. While case 16 escaped gastrointestinal disturbances, there was no maintained circulatory advantage.

To throw further light on the problem of the balance between therapeutic advantages and the toxic drawbacks in the use of thevetin it was thought important to analyze the clinical data in this group of patients from the standpoint of the initial effect of the drug. This analysis is presented in table 2. At a glance it will be seen that in only three patients (cases 1, 11 and 20) did the toxic manifestations anticipate the therapeutic action of

the drug. Interesting though this circumstance may be, it loses some of its significance when the necessity for a protracted action in this group of patients is called to mind. Hence a summary of the ultimate effects of thevetin therapy is shown in table 3.

It will be seen from this table that 19 of the 25 patients experienced a desired circulatory response from the oral use of reduced doses of thevetin and that two patients (cases 4 and 6) were assessed as doubtfully improved. In the remaining four (cases 1, 11, 16 and 20) no appreciable advantage from the use of the drug was observed. These results are comparable with those obtained when the routine of the Eggleston tolerance dosage was conformed to in the use of thevetin.[2] More interesting is the analysis of the adverse reactions under the reduced scale of dosage. Here it appears that 18 of the 25 patients were free from untoward symptoms and seven experi-

TABLE III

Summary of Ultimate Effects of Thevetin from Table I

	Clinical Observations	Total	Case Numbers
Circulatory Condition	Improvement	19	2, 3, 5, 7, 8, 9, 10, 12, 13, 14, 15, 17, 18, 19, 21, 22, 23, 24, 25
	Doubtful improvement	2	4, 6
	No response	4	1, 11, 16, 20
Untoward Symptoms	Symptoms absent or negligible	18	2, 3, 5, 7, 9, 10, 12, 13, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25
	Gastric symptoms, only (anorexia, nausea, vomiting)	0	
	Intestinal symptoms, only (cramps, diarrhea)	3	8, 11, 14
	Both gastric and intestinal symptoms	4	1, 4, 6, 20

enced either intestinal distress or intestinal and gastric disturbances. In two patients (cases 8 and 20) diarrhea was controlled upon lowering the dosage of thevetin. In a third (case 14) the circulatory advantage was maintained, but the glucoside was eventually discontinued upon the occurrence of a slight diarrhea (without recourse to the simple expedient of lessening the dose). Obviously then in only four instances (cases 1, 4, 6 and 11) may thevetin be charged with adverse gastrointestinal effects of such degree as to preclude its continued use and in each instance it will be observed that cramps accompanied the diarrhea. It has been our experience with larger, as well as with reduced doses of thevetin that a mild diarrhea constitutes no sound objection to the continuance of the drug. Indeed, there may be some advantage through the reduced physical effort of defeca-

tion. Moderate to severe diarrhea and cramps, however, constitute as serious handicaps as do nausea and vomiting.

When compared with the adverse results of thevetin therapy under an Eggleston regimen of dosage by body weight,[2] there is a distinct advantage in favor of the reduced doses. Twenty-four of the earlier group of 40 patients (60 per cent) were free from symptoms as compared with 18 of 25 patients (72 per cent), in the present group. Obviously the reverse of the picture is true, namely a higher incidence of gastrointestinal symptoms on the larger doses of thevetin than with schedule of reduced doses (40 per cent against 28 per cent). Apparently there is an individual idiosyncrasy to thevetin particularly in the occasion of intestinal cramps and this circumstance determined a small group in this series of patients, as well as the earlier groups, to whom thevetin was denied for this reason alone.

The therapeutic-toxic ratio of digitalis-like drugs is so important that a search of the literature was made for studies of this type upon digitalis itself. Generalities were found to prevail, but Bastedo [6] reported a 35 per cent incidence of toxic symptoms among 90 patients receiving digitalis in Bellevue Hospital. Whereupon Shanahan [7] undertook an analysis of the matter from the materials in the records of the Wisconsin General Hospital. A careful selection of materials was made to exclude those with prior digitalis therapy, inadequate control observations or other confusing factors. Among a group of 65 patients with cardiac decompensation thus culled from a large series, he found that 37 per cent showed some evidence of digitalis intoxication at one time or other. Furthermore 28 per cent of these 65 patients developed symptoms of the toxic action of digitalis before any circulatory advantage was attained. Finally 22 per cent of the group showed such serious reactions to digitalis as to preclude its continuance.

These figures are not quoted in extenuation of the untoward results from thevetin therapy. Apparently a reduction of the dosage of this glucoside by mouth commensurate with its superior vagal effect has induced a lessening of the gastrointestinal action. Nevertheless cramps and diarrhea do occur in an appreciable percentage of cases even under reduced doses. In some of these, the adverse effects do not outweigh the circulatory advantage incident to the use of thevetin. In others, the toxic symptoms preclude further use of the drug. On the other hand in cardiac cases that do not tolerate digitalis well thevetin may offer the boon of a further reliable cardiac glucoside. Moreover as has been reported earlier [1] thevetin possesses distinct advantages as a drug for emergency use by intravenous injection.

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THE DIAGNOSIS AND TREATMENT OF HYPER-INSULINISM *

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THE recently recognized disease entity, hyperinsulinism, is being diagnosed with increasing frequency. Cases have been reported in practically every country in the world in which medical journals are published. It is interesting to observe the influence of American medical literature on clinical practices in foreign countries; and it is pleasing to note that, in nearly all the articles on hyperinsulinism and spontaneous hypoglycemia in foreign journals, the authors have been generous in their references to contributions on the subject by American physicians.

Among the many foreign clinicians who have reported cases of hyperinsulinism, or spontaneous hypoglycemia, or have published articles on the subject, may be mentioned: Cammidge (1924 and 1930), Cameron (1930), Wauchope (1933), Cairns and Tanner (1933), of England; Moore, O'Farrell and Malley (1931), of Ireland; Sippe and Bostock (1933), of Australia; Posel (1933), of South Africa; Gougerot and Peyre (1925), Sendrail and Planques (1927), Laroche, Lelourdy and Bussiere (1928) and Sigwald (1932), of France; Krause (1930), Roth (1930), Wilder, Josef (1930) and Rosenberg (1932), of Germany; Bakser (1933), of Poland; Federoff (1931), of Russia; Stenstrom (1926), Sjogren and Tillgren (1927), Hagedorn (1932), Ehrström (1932), of Scandinavia; Massa (1929), Reale (1929), Lami (1930), Cimmino (1931), and Tarsitano (1931), of Italy; Zubirian (1929), of Mexico; and Valenzuela (1931), of Chile.

Hyperinsulinism Consciousness. "Hyperinsulinism takes another syndrome from the waste basket of neuroses" is the syllogistic statement of Evans and McDonough, of LaCrosse, Wisconsin, who found and relieved six cases in six months' private practice after they became "hyperinsulinism conscious."

Powell, a general practitioner of West Monroe, Louisiana, found 25 cases of hyperinsulinism in two years after he recognized his first case. He concludes: "Ample case reports are now in the literature to show that hyperinsulinism causes symptoms varying from drowsiness to narcolepsy, from vertigo to epilepsy, and from mental deficiency to mental degeneracy. Unfortunately all the cases are not in the literature—they are to be found in every doctor's clientele and, sad to relate, are most probably untreated.

Wilder, Allen, and Robertson, in 1927 made autopsy studies of an inoperable case of hyperinsulinism due to an islet cell carcinoma, and proved the pathological basis for the condition. Since then Wilder, Allen, Judd,

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Rowntree, Rynearson and their associates have reported a number of cases, most of which have been operated upon. Wilder called attention to the erroneous diagnoses as applied to hyperinsulinism, including "nerves, neurasthenia and hysteria." He adds: "Hypoinsulinism and hyperinsulinism are in fact clinical antitheses: the latter is of as serious significance as the former, and the practitioner of today must be as familiar with one as with the other."

Marsh, of Madison, Wisconsin, who reported eight cases of mild hyperinsulinism in 1931, regards the condition as of frequent occurrence. Tedstrom, of Santa Ana, California, reported four cases and analyzed the literature on 64 other cases in 1933. In 1935 he states that he has had about 100 cases of hypoglycemia, most of which are due to hyperinsulinism.

It is not an accident that Carr, Parker, Larrimore, Graham, Womack, Marriott and their associates in Barnes Hospital (Washington University) in St. Louis, since 1930 have diagnosed and have removed five islet adenomas, and have performed three resections of the pancreas for hyperinsulinism, thus relieving patients of otherwise hopeless conditions. One of the most dramatic cases in surgical literature is Evarts Graham's first subtotal pancreatectomy in a 15 months old baby, whose condition was hopeless because of mental deterioration and convulsions due to hyperinsulinism. The child has had no convulsions since the operation and his mentality, as studied by scientific tests, has improved 40 to 50 per cent. Graham and Womack are impressed with the neuro-psychiatric manifestations of hyperinsulinism. After discussing various symptoms they conclude: "It is important to emphasize that in many cases the neurological and psychiatric aspects of the condition are so prominent that many of the patients with chronic hypoglycemia have been referred primarily to neurologists and psychiatrists for treatment."

About one year ago Whipple in the Presbyterian Hospital, New York, removed an islet cell adenoma from a patient who had recurring attacks of unconsciousness, and other nervous and psychic phenomena, associated with hypoglycemia, with dramatic relief of symptoms. When the staff of the Neurological Institute of the Presbyterian Hospital became "hyperinsulinism conscious" they found five similar cases upon which Whipple operated with clinical cures. Thus six persons, who were doomed to institutional lives as psychotics, or to die in hypoglycemic coma, were restored to health by the coöperation of the neuro-psychiatric and surgical staffs of one hospital. No doubt there are as many cases of hyperinsulinism passing, unrecognized and unrelieved, through the wards of every other large hospital in the country as were diagnosed and cured at the New York Presbyterian Hospital during the last 12 months.

Winans in Dallas, Texas, and Waters in Atlanta, Georgia, have reported a number of mild cases of hyperinsulinism which they relieved by dietary management. Winans in a recent paper on insomnia called attention to hypoglycemia as one of the causes of sleeplessness.

In Toronto, Howland, Campbell, Maltby, and Robinson in 1929 made the first preoperative diagnosis of an islet tumor, the removal of which cured the patient of convulsions due to "dysinsulinism." Rabinowitch, in Montreal has reported five cases of hyperinsulinism. Goldzieher of New York recently reported 200 cases of spontaneous hypoglycemia. Many other cases have been reported by American clinicians, and many more have been recognized and treated by physicians who have become "hyperinsulinism conscious" but have not reported their cases.

Cammidge, of London, stimulated by his recognition of two cases of "chronic hypoglycemia" in 1924—an observation that no doubt was independent of the work done by others—found 198 additional cases before 1930, an average of 33 cases a year. The fact that Cammidge has reported more cases of spontaneous hypoglycemia than all the other clinicians in the British Empire means simply that he learned to recognize the symptoms due to hypoglycemia and clinched his diagnoses by finding low blood sugars. However, a number of cases have been reported by other British clinicians. Sippe and Bostock in Brisbane, Australia have reported 30 cases of chronic hypoglycemia. They regard the condition as being almost, if not quite, as frequent as the opposite condition, diabetes mellitus (hypoinsulinism). They observed hypoglycemia in 0.47 per cent of their patients, while diabetes was diagnosed in 0.51 per cent.

Recently Sippe reported five cases of hypoglycemia associated with angina pectoris. Cardiographic studies and blood sugar determinations showed correlation of the cardiac symptoms to hypoglycemia. The cardiac attacks were prevented, or relieved, by a diet that maintained, or raised, blood sugar levels above the point at which the cardiac manifestations of hypoglycemia appeared.

Personal Cases. From March 1923 to May 1935 I have made the clinical diagnosis of hyperinsulinism in 119 cases, an average of 9.9 cases a year. In a number of these cases the diagnosis of hyperinsulinism was made by other physicians before they referred them to us for treatment. In none of these cases could we find evidence of any liver disorder that could cause hypoglycemia, though in several cases there were manifestations of dyspituitarism, in the stage of hypofunction, hypothyroidism and hypoadrenalism which seemed to have been the primary cause of the relative, or actual, hyperinsulinism responsible for the hypoglycemic symptoms.

Without question many hypoglycemic patients pass, untreated and unrelieved, through the hands of capable clinicians, because they have not become "hyperinsulinism conscious." The opinions of a number of physicians, who have had experience in dealing with hyperinsulinism, have been cited to prove that the condition, or disease entity, must be reckoned with by the medical profession. It therefore seems timely to discuss the diagnosis and treatment of hyperinsulinism.

Anamnesis. Evidence favoring the diagnosis of hyperinsulinism may sometimes be elicited in patients who complain of "spells" of various kinds,

by inquiring as to whether the attacks occur during the night, before breakfast, or several hours after meals. If such is the case and if the patient's symptoms are relieved by taking a soft drink, fruit, or milk, or other food between meals, and if the patient feels distinctly more comfortable after meals, one would suspect hyperinsulinism. My early cases were of that type. Sometimes, however, the hypoglycemic attacks seem to occur at meals, at the sight of food, or immediately after leaving the table before there is time for digestion and assimilation of carbohydrates and when the blood sugar is still low.

Hyperinsulinism has been called the "hunger disease," because excessive appetite and the desire for food between meals are present in most cases. Sometimes, however, the patient with hyperinsulinism becomes nauseated when the attacks of weakness, nervousness and even unconsciousness occur. The patient may also complain of abdominal discomfort, relieved by taking food, his symptoms thus resembling those of gastric or duodenal ulcer. Several such cases in which operation for peptic ulcer had been considered have come under my observation.

Hunger and relief of symptoms by eating are not sufficient evidence to warrant a diagnosis of hyperinsulinism. I have seen two cases of pronounced bulimia, one in a hysterical woman and another in a mild psychotic, who obtained temporary relief from eating, but whose glucose tolerance blood sugar curves were normal.

A history of over-indulgence in sweets of all kinds is frequent in patients with hyperinsulinism. Not infrequently the victim of this condition has learned that he can relieve his symptoms by eating sweets and he devours candy and various "nick nacks," between meals to keep off attacks. After a time sweets give relief for only a few minutes. Often such patients will voluntarily mention that they "crave sweets." Occasionally hyperinsulinism patients will go on "sugar sprees" when they will eat inordinately of cakes, candy, pies, ice cream and other cane sugar products for a few days. Usually their symptoms are aggravated by such overindulgences.

Overindulgence in Sweets and in Caffeine Beverages. My first case of hyperinsulinism observed 12 years ago gave a history of overindulgence in caffeine beverages. Since then the history of taking coca-cola, or coffee, between meals for the relief of the attacks of hypoglycemia, or to prevent them, has occurred too frequently not to have a relationship of cause and effect; at least the symptoms are exaggerated by the frequent use of soft drinks between meals. The caffeine soft drinks relieve the symptoms temporarily; first, by supplying a soluble carbohydrate that is rapidly absorbed and metabolized; and second, as Womack suggested, probably by the stimulation of the adrenals by caffeine, thus raising the blood sugar level above the point at which the hypoglycemic symptoms occur.

A good therapeutic test for hyperinsulinism is to give the patient a glass of coca-cola, or a cup of coffee without cream, during an attack, or before the suspected attack. If it relieves the symptoms temporarily or prevents

the attacks, hyperinsulinism may be suspected. Certainly there is not a better or quicker acting remedy for an attack, or for symptoms of hypoglycemia, than a glass of coca-cola or other caffeine-containing soft drink, or a cup of coffee, with sugar but without cream. The regular excessive use of the caffeine beverages, however, seems to exaggerate the hypoglycemia in patients with hyperinsulinism.

Gastrointestinal Manifestations. The gastrointestinal manifestations of hyperinsulinism are frequent and varied. A considerable proportion of the patients who have hypoglycemic symptoms associate their discomfort with food. Often they feel that certain articles of food they had eaten previous to attacks were responsible for their symptoms. Many such patients complain of hunger, but sometimes they suffer from sitophobia because of the fear that eating will make them worse.

Many patients who have come to our clinic complaining of "nervous indigestion," or with a previous diagnosis of "irritable colon," have been found to have hypoglycemia that synchronized with their symptoms, and have been relieved by a diet planned to keep blood sugar levels within normal limits. Other patients, with actual duodenal ulcers, have had associated nervous symptoms which were proved to be due to hypoglycemia. It, therefore, should be remembered that hyperinsulinism may coexist with actual lesions of the stomach and other abdominal viscera.

Cammidge in reporting 200 cases of "chronic hypoglycemia" said: "Comparatively few cases of hypoglycemia are free from gastrointestinal disorders." Sippe and Bostock mentioned gastrointestinal symptoms in 18 of 25 reported cases of "chronic hypoglycemia," most of them mild cases that were promptly relieved by dieting. Many other clinicians have reported cases of hyperinsulinism, or chronic hypoglycemia, in which gastrointestinal symptoms were present.

Dextrose tolerance tests, carried out for six full hours, in patients with complaints referable to the gastrointestinal tract, associated with nervousness and weakness, may reveal hypoglycemia as the cause of the symptoms.

Abdominal Pain. Evarts Graham observed abdominal pain in his first case of islet cell adenoma of the pancreas. The patient had had his appendix removed without relief from the abdominal pain. Abdominal pain, however, is by no means a constant symptom in the severe cases of hyperinsulinism with, or without, adenomas of the pancreas. Womack writes: "In two of eight cases, five adenomas of the pancreas and three resections successfully operated upon in Barnes Hospital, pain in the abdomen was outstanding. A cholecystectomy was done in one elsewhere and an appendectomy in the other with no relief. This cramp-like pain disappeared with the relief of the hypoglycemia." Undoubtedly many unnecessary and unsuccessful abdominal operations have been performed upon hyperinsulinism patients.

The location of the pain is important. In the cases of hyperinsulinism that I have seen, in which abdominal pain was a symptom, the pain was in

the mid-portion and upper left quadrant of the abdomen. In most of them there was tenderness on deep pressure in the same locality, i.e., over the pancreas. Periodicity of the pain, usually more pronounced when the stomach was empty, was present in a number of cases. Partial resections of the pancreas relieved the pain in three of my cases.

Attacks of Convulsions and Unconsciousness. The most important manifestations of the severe types of hyperinsulinism are attacks of unconsciousness and convulsions. Most of the patients with hyperinsulinism who have been operated upon have had varying periods of unconsciousness, with and without convulsions; and many of them have been diagnosed as epilepsy, until blood sugar studies proved the presence of a sufficient degree of hypoglycemia to account for the convulsions and unconsciousness.

Convulsions do not occur in all severe cases of hyperinsulinism: frequently attacks of unconsciousness resembling diabetic coma occur. Several cases of death in hypoglycemic coma without convulsions have been reported and the diagnosis was proved by finding at autopsy tumors of the islands of Langerhans.

The unconsciousness following hypoglycemic convulsions lasts from a few minutes to several hours. In one case of repeated convulsive attacks, in which the patient was in what was called "hypoglycemic status epilepticus" a clinical cure resulted from the removal of a carcinoma of the islands of Langerhans (Bast, Schmidt and Sevringhaus). Often patients with hyperinsulinism awaken voraciously hungry after convulsions; but not always, because nausea and vomiting sometimes follow hypoglycemic attacks.

Hysterical and Psychotic Manifestations. Many patients who have been regarded as hysterical, or psychasthenic, have been proved to suffer from hyperinsulinism, and have been clinically cured by regulation of the diet.

Actual psychotic symptoms may occur in the severe cases of hyperinsulinism. The woman, reported by Finney and Finney, had "crazy spells" when she would do queer things. She was found to have a blood sugar of 0.030 per cent. Graham and Womack reported cases in which patients with hyperinsulinism had actual psychoses which subsided after removal of islet cell adenomas of the pancreas. Many other clinicians have observed psychotic patients who had hyperinsulinism.

Powell suggests that the protean nervous manifestations in hyperinsulinism are due to a deficiency of glucose in the blood supply of the brain. He cites a recent editorial in the *Journal of the American Medical Association* to the effect "that the brain lives exclusively on a sugar diet and that the quantity thereof may readily be determined by various blood sugar and glucose tolerance tests." Zeigler says that spontaneous hypoglycemia will cause insomnia and maniacal delirium.

Diagnosis

A positive diagnosis of hyperinsulinism either of the mild or severe type cannot be made without fasting blood sugar studies and glucose tolerance tests proving the presence of hypoglycemia in a patient with symptoms of hyperinsulinism.

Routine fasting blood sugars on my patients for the last 12 years have shown hypoglycemia in many whose history did not suggest hyperinsulinism; but who, on more careful questioning, gave definite hypoglycemic symptoms. In my first case of epilepsy associated with hyperinsulinism the diagnosis was not suspected until his fasting blood sugar, taken as routine, was found to be 0.060 per cent. Attention having been called to the low fasting blood sugar in this case, further questioning brought out a history of hypoglycemic symptoms; and then a glucose tolerance test showed a low flat hyperinsulinism curve.

Repeated Blood Sugar Studies. One fasting blood sugar or one glucose tolerance test is not always sufficient to warrant a positive diagnosis of hyperinsulinism since there seem to be periods when the hyperinsulinism patient will have normal blood sugar readings, even though at other times he has shown marked hypoglycemia. Cushing observed in hyperpituitarism that there are undulations, or waves of accelerated hypophyseal secretion; and it is quite evident that in hyperinsulinism there are quite marked variations in islet cell secretion.

The factor of mental and physical fatigue affects blood sugar levels. In making glucose tolerance tests, ambulatory patients should not be permitted to lie down, but should, if possible, take about the same amount of exercise that they ordinarily take when the attacks have occurred. I have observed repeatedly in patients taking the glucose tolerance test that when the blood sugar levels became low, they had hypoglycemic symptoms which subsided when they lay down. After resting for a few minutes without taking food, the blood sugar readings were higher.

The occurrence of the symptoms complained of, at the stage of the test when the blood sugar becomes low, as frequently occurs, is presumptive evidence of hyperinsulinism. So likewise is the finding of a low blood sugar in blood drawn during a spontaneous attack. It, therefore, is advisable to get repeated blood sugar tests an hour before the noon and evening meals and after the patient has had several hours' work at his usual vocation at about the time symptoms usually occur. In studying patients with a history of epileptic or epileptiform attacks, blood sugar tests should be made at about the time of expected attacks; but it should be remembered that after generalized convulsions usually the blood sugar readings will be higher than before the paroxysm.

Gammon and Tennery suggested that in examining the patient suspected of having hyperinsulinism sufficient insulin be given to produce hypoglycemic reactions which in many cases will reproduce the patient's symptoms.

Since in many cases the same result may be accompanied by reproducing the symptoms in the hypoglycemic phase of glucose tolerance tests, the use of insulin as a diagnostic measure seems rarely indicated.

The Six Hour Glucose Tolerance Test. The glucose tolerance test should be carried out for six full hours in making the diagnosis of hyperinsulinism. I have observed a number of patients whose blood sugar readings were normal for four hours after the ingestion of the dextrose, but fell rapidly and to very low levels in the fifth and sixth hours. Recently a patient who had marked symptoms of hyperinsulinism and had shown a hyperinsulinism curve was given a glucose tolerance test in another hospital. The test was carried out for only four hours, the last reading having been 0.070 per cent; on this evidence the case was not diagnosed as hyperinsulinism. Four hours is long enough to carry out a glucose tolerance test for diabetes, but six or eight hours may be necessary in studying the case for suspected hyperinsulinism. If glucose tolerance tests were carried out for six hours, they might show, as they did in a few of my cases, a diabetic curve for three or four hours and hypoglycemic readings for the fifth and sixth hours.

Patients object to and sometimes refuse venupunctures for blood specimens every hour for six hours, and laboratory technicians sometimes get tired of running blood sugars; but unless the test is carried out that long, some cases of hyperinsulinism will not be diagnosed as such. Sometimes it is difficult to get into the veins in making glucose tolerance tests, and then it is best to get the fasting blood sugars and the blood sugar five and six hours after the ingestion of the dextrose.

Therapeutic Test. If for any reason the patient cannot or will not have blood sugar studies made and if hyperinsulinism is suspected, a few days of rest on a relatively low carbohydrate diet consisting largely of the 5 and 10 per cent vegetables and fruits, with orange or tomato juice on arising and on retiring and every one or two hours between meals and when awake at night, may relieve the symptoms. If the patient is underweight, two to four ounces of cream may be given every three hours when awake. The cane sugar products and other soluble carbohydrates including soft drinks and candy between meals should be given only to relieve the attacks. On such a diet with sufficient rest, the patient with all but the most severe hyperinsulinism will be improved or completely relieved of his symptoms. If he is not relieved either his symptoms are not due to hyperinsulinism or blood sugar studies may show hypoglycemia of sufficient degree to demand exploration of the pancreas for an adenoma.

The Diagnosis of Hypoglycemic Coma. It should be a routine in every case of unexplained unconsciousness to make a blood sugar determination at the earliest moment possible. Hypoglycemic coma is one of the frequent causes of unconsciousness, particularly when preceded by convulsions. Wauchope recommends the use of adrenalin hypodermatically, and dextrose intravenously in the cases in which there is the question of diabetic or hypo-

glycemic coma. If the unconsciousness is due to hypoglycemia the adrenalin and the dextrose intravenously will bring the patient out of the coma in a few minutes; whereas if the patient continues unconscious a delay of 15 minutes while waiting for a blood sugar report will not affect the ketosis which usually can be relieved by the use of insulin.

Differential Diagnosis

Every possible cause of hypoglycemia besides pancreatic disease should be considered, including studies of all the other organs of internal secretions, so as to exclude them as factors if possible, before making a diagnosis of uncomplicated hyperinsulinism.

Since hyperinsulinism has been manifested by symptoms which have suggested hysteria, psycho-neurasthenia, neuro-circulatory asthenia, psychoses, brain tumors, epilepsy, narcolepsy, status epilepticus, epileptiform convulsions, appendicitis, gall-bladder infection, duodenal ulcer and many other diseases it is apparent that in the study of all patients presenting such symptoms blood sugar tests should always be included. On the other hand the finding of hypoglycemia does not always prove that it is the cause of the symptoms. We have had two cases of brain tumor in which hypoglycemic symptoms were pronounced.

Hyperinsulinism is invariably associated with hypoglycemia. It should be remembered, however, that in patients who have hypoglycemic symptoms, fasting blood sugars are not always low. Therefore, repeated and varied blood sugar studies should be made before hypoglycemia is excluded in suspected cases of hyperinsulinism. It should be remembered also that the patient with hyperinsulinism may have other diseases that may, or may not, affect the hypoglycemic symptoms. Thus, two cases of hyperinsulinism in syphilitic patients have been observed in which anti-syphilitic treatment did not affect the blood sugar levels or the symptoms of hypoglycemia.

Hypoglycemia from Extra-Pancreatic Disorders. Cases of marked degrees of hypoglycemia due to organic diseases or functional disturbances of other organs besides the pancreas have been reported as having been due to (*a*) a deficient glycogenesis in the liver from poisons such as arsphenamine or other arsenicals, phenylhydrazine, phosphorus or other hepatotoxins (Cross and Blackford), and from massive tumor of the liver (Nadler and Wolfer); (*b*) inadequate mobilization of glycogen due to deficient secretion of the suprarenals (Anderson); (*c*) pituitary dysfunction (Josef Wilder); (*d*) thyroid dysfunction (Tedstrom). The case of Weil, in which the hypoglycemic convulsions occurred only during menstruation suggests that ovarian dysfunction may be a factor in some cases.

It is of particular importance to exclude hypopituitarism, hypothyroidism, and hypoadrenalinism which may be the primary cause of the hypoglycemia that is responsible for the symptoms of hyperinsulinism. The secretions of the hypophysis, thyroid and adrenals are antagonistic to, and therefore may control, the secretion of insulin.

Treatment

The problem of dieting in hyperinsulinism is much the same as in diabetes mellitus (hypoinsulinism) in that each patient has to be dieted to suit his particular needs. It is necessary to arrange a diet that will nourish the patient properly, providing sufficient amounts of carbohydrates, proteins and fats, with due consideration to its vitamin content. As far as the quantity is concerned, it should have a lower carbohydrate content than in diabetes, with sufficient calories to maintain normal body weight and physical vigor. The protein content should depend on the age and weight of the individual; we give from 60 to 75 gm. to an adult weighing 70 kilograms.

Theoretically, a high carbohydrate diet would seem to be indicated in hyperinsulinism, but John pointed out that carbohydrates stimulate the secretion of insulin and that when rapidly soluble carbohydrates such as sugars are given, they cause excessive insulogenesis, which continues after the carbohydrates are metabolized, with resulting hypoglycemia. John observed, in giving dextrose tolerance tests, that while the blood sugar level was high for the first one or two hours, it was followed by a rapid fall to a level much lower than the fasting blood sugar. I made the same observation independently after giving a dextrose tolerance test to my second patient with hyperinsulinism in 1923.

Weil's experience with his patient with dysinsulinism, who had recurring attacks of convulsions and unconsciousness, proves the fallacy of a diet high in soluble carbohydrates in insulogenic hypoglycemia. He found that a few hours after a high carbohydrate meal, the blood sugar reached a much lower level than the patient's fasting blood sugar. He was able to control the attacks of convulsions by placing the patient on a low carbohydrate, high fat diet with frequent feedings.

Shepherdson states that the blood sugar level will rise on a low carbohydrate, high fat diet. He quotes Weeks, Renner, Allan and Wishart as having observed in a study of epileptic patients on high fat diets that in every case they developed a hyperglycemia. It is possible that ingested fats may have a direct effect in inhibiting the secretion of insulin and that, in the cases of epilepsy associated with hypoglycemia in which the ketogenic diet has proved beneficial, perhaps in some cases the good effects have been due to a rise in the blood sugar level, rather than to the sedative action of the ketone bodies in the blood. Certainly in my hands a moderately low carbohydrate, high fat, moderate protein diet has given the best results in treating chronic hyperinsulinism.

Low Carbohydrate, High Fat Diets. Early in my experience in dealing with hyperinsulinism I began using a low carbohydrate diet, consisting largely of 3, 5 and 10 per cent vegetables and fruits, combined with a high proportion of fats, with frequent feedings. I reasoned that the carbohydrates in the form of vegetables and fruits, which must be digested before being absorbed and metabolized would be released as dextrose in small

quantities at a time, and therefore, would not stimulate the secretion of insulin as much as meals made up largely of foods of high carbohydrate content, particularly those containing cane sugar products. Fats, particularly cream, were given with meals and between meals, with the idea that they are emptied slowly from the stomach. Therefore, the metabolism of the carbohydrates mixed with fats would be slow compared to the rapid emptying of the stomach and the accelerated metabolism after the ingestion of carbohydrate meals without fats.

Waters, basing himself upon the experimental studies of Sweeney, which showed higher blood sugar levels after high fat diets, and lower levels after high carbohydrate diets, and also upon his own experience in relieving cases of spontaneous hypoglycemia by a high fat, moderately low carbohydrate diet, concluded: "A diet reducing the carbohydrate intake and increasing the volume of fats seems to diminish an excessive insulin production and to raise the blood sugar level."

Dieting the Hyperinsulin Individual. The diet in each case of hyperinsulinism should be calculated to meet the patient's nutritional needs. The adult patient with hyperinsulinism, of average height and weight, should have about 2,250 calories, derived from 90 to 150 gm. of carbohydrates, from 60 to 75 gm. of proteins and the remainder from fats, largely cream and butter. The food intake is best divided into from five to seven feedings a day.

A number of my patients with hyperinsulinism have been overweight, and other clinicians have observed a number of obese patients with hyperinsulinism. In such cases the fats should be reduced, and a low caloric diet with food every two hours is indicated. In such cases I prescribe a diet of about 120 gm. of carbohydrates, 60 gm. of fat and 60 gm. of protein (1,260 calories) divided into six or eight feedings a day. On such a diet the patient's activities should be restricted and the amount of carbohydrates should be increased to 150 to 200 gm., or even more if the patient is losing weight, or if he becomes weak.

In the underweight, asthenic patient with hyperinsulinism, a diet of 90 to 150 gm. of carbohydrate, from 200 to 300 gm. of fat, and from 60 to 75 gm. of protein, divided into five or six feedings a day, will keep the blood sugar at a sufficiently high level to prevent hypoglycemic symptoms, and will build up the patient's general health and state of nutrition.

Careful blood sugar studies should be made on each patient for a few days after being placed on a diet for hyperinsulinism, during which time his food should be weighed and measured if possible. It is just as necessary to teach the patient with hyperinsulinism food values and to calculate and arrange the menus suited to his particular case, as it is to teach "diabetic arithmetic" to patients with hypoinsulinism (diabetes mellitus). The intelligent patient with severe hyperinsulinism usually becomes very much interested in "playing the game of dieting" because he has a holy dread of the attacks of unconsciousness, with or without convulsions.

It is essential to impress the patient with hyperinsulinism with the necessity of moderation in all things, particularly physical exercise. Studies on marathon runners by Levine and his associates showed that physical exhaustion produces physiologic hypoglycemia. A number of my patients have observed that their attacks of hunger, weakness and the like, and even petit mal and grand mal seizures, have occurred most frequently after physical exertion. The patient with hyperinsulinism should be taught all the rules of personal hygiene adapted to his particular needs, just as the diabetic patient is taught how to live and enjoy health even though he has the handicap of a crippled pancreas.

The Use of Bromides and Barbiturates in Hyperinsulinism. The dietary management of hyperinsulinism, without medicines, usually is sufficient to control the disease and prevent hypoglycemic symptoms in the mild types and in many of the severe cases; yet drugs may be required at times in the more serious cases, particularly in those associated with epileptiform convulsions.

The rationale of the use of the bromides and barbiturates in epilepsy is considered to be their effect as motor depressants, thus preventing the convulsions. We are studying, as clinical material becomes available, the question as to whether these drugs may have some effect in raising the blood sugar in severe hyperinsulinism. The bromides are not advised in the treatment of hyperinsulinism, even when it is associated with epilepsy, except as a temporary measure. The bromism that follows the use of the bromides when used over a long period of time may be more harmful to the epileptic patient with hyperinsulinism than the convulsions. Phenobarbital in 1½ grain (0.1 gm.) doses night and morning and in the most severe cases after the noon meal is the least harmful drug now known that will control the epileptic convulsions; and it is helpful in cases of severe hyperinsulinism in patients who cannot, or will not, follow a prescribed diet. Phenobarbital may be used in conjunction with dietary management in cases that are difficult to control.

Belladonna. Having in view the possibility that belladonna might inhibit the secretory activity of the islet cells, I have used it in my mild cases of hyperinsulinism for several years, at times with seemingly good results.

Evans and his associates report the discovery of a diabetogenic hormone from the anterior pituitary, which will raise blood sugar. As yet this hormone has not been separated from the growth, and perhaps other, hormones; but there seems reason to hope that a purified product of the diabetogenic hormone will be available for use in hyperinsulinism in the near future.

Suprarenal Products. Adrenalin (1 c.c. of 1–1000 solution) given hypodermatically will raise blood sugar, and in hypoglycemic coma may restore consciousness in a few minutes; but its effects are temporary and it is not of value in hyperinsulinism except in the attacks. Adrenalin has no effect when given orally, and it is questionable if any of the preparations

of suprarenal medullary substance are of value if given by mouth. Nielsen and Eggleston, however, credited a whole gland product of the suprarenals with a part of their successful treatment of three cases of epileptiform convulsions due to "dysinsulinism."

Ephedrine. Ephedrine has been used successfully in the treatment of narcolepsy. Ephedrine mobilizes glycogen and, combined with diet and rest, may maintain the blood sugar level at a point high enough to prevent hypoglycemic symptoms. Ephedrine was used with doubtful results in two of our cases of epilepsy with hyperinsulinism.

Thyroid Extract. Since hypothyroidism is sometimes associated with hyperinsulinism, thyroid extracts would seem to be indicated in the cases in which the basal metabolic rate is low. Tedstrom, and Evans and McDonough used thyroid extracts with benefit in the treatment of some of their cases of hyperinsulinism with low basal metabolic rate.

Insulin. John reports having used insulin with excellent results in the treatment of hyperinsulinism. He is of the opinion that if exogenous insulin is given hypodermatically after meals before the postprandial blood sugar rise stimulates the secretion of insulin, the amount of endogenous insulin will be sufficiently reduced so that the hyperinsulinism patient will not become hypoglycemic several hours after meals. John gives from 10 to 20 units of insulin after meals and presents blood sugar records before and after the insulin was used, which seem to justify his conclusions. I have used insulin in two cases of hyperinsulinism with apparently good clinical results, though blood sugar studies were not made to prove that the blood sugar levels were higher after the use of insulin.

Deep Roentgen-Ray Therapy. Barrow has used deep roentgen-ray therapy in the treatment of hyperinsulinism with reported good results. He believes that the irradiation over the pancreas may reduce the secretion of insulin just as it sometimes ameliorates the symptoms in hyperpituitarism with or without adenomas, presumably by decreasing hypophyseal secretion In view of possible dangerous secondary irradiation of the liver, stomach, duodenum and other neighboring organs, this therapeutic method should be used with great caution in attempting to decrease insulin secretion. Sippe and Bostock quote Terbruggen and Heinlein as having "produced a lethal hypoglycemia in rabbits by irradiation of the pancreas." The external secretory portion of the organ, involved in producing trypsin, amylopsin and steapsin showed degenerative changes; whereas the islands of Langerhans were well preserved or even hypertrophic. Mosenthal also mentions irradiation of the pancreas as having caused hypoglycemia.

Surgery in Hyperinsulinism

While the mild and moderately severe, and many of the very severe cases of hyperinsulinism can be relieved by dietary management, as certainly as diabetes mellitus can be controlled by diet and the use of insulin, in an oc-

casional case surgery offers the only hope of relief. The question then arises: When is surgery indicated in hyperinsulinism?

It should be stated emphatically that in no case of hyperinsulinism should surgery be resorted to until the patient has given a full trial to properly directed dietary management. Haphazard dieting in hyperinsulinism gives as unsatisfactory results as unscientific methods in the management of diabetes mellitus; so that the patient with hyperinsulinism has not had the best chance to control his disease unless he has been kept, for a few weeks at least, on a weighed and measured diet calculated and prescribed to suit his individual needs. If the hyperinsulinism patient cannot control his symptoms by properly directed dieting then surgery should be considered.

It is an interesting fact that of the 40, or more, operations on the pancreas for hyperinsulinism all but two have been performed by surgeons in the United States and Canada. There has not been a death reported from pancreatic operations performed in the United States, though I have heard of two deaths which resulted from operation that have not been reported. The only two operations on the pancreas for the relief of hyperinsulinism that have been reported, besides the American cases, were performed in Russia; both died from the operations. In one of these, a large adenoma of the pancreas, the growth had reached the stage where it was inoperable.

Criteria for Exploratory Operations. An exploratory operation for the relief of hyperinsulinism should be considered:

1. In the acute fulminating cases which develop rapidly and in which hypoglycemic attacks with convulsions and unconsciousness cannot be controlled by intravenous dextrose therapy, and in which death seems imminent.
2. In the severe chronic cases that cannot be controlled by properly directed dietary management in a few weeks.
3. In cases with severe neuro-psychiatric symptoms of long standing in which on account of economic or social or psychic handicaps the diet cannot be carried out properly, or long enough to permanently benefit the patient.

Surgery of the pancreas is contraindicated in primary disease, or hypofunction, of the anterior pituitary, the thyroid, or the adrenals, resulting in relative, or actual, hyperinsulinism, for the obvious reason that such operations could not remove the cause of the hypoglycemic symptoms. Likewise no benefit could be expected from surgery in hypoglycemia resulting from acute yellow atrophy of the liver, massive carcinoma of the liver, or the hepatic lesions that follow acute poisoning from hepatotoxins such as arsphenamine, phenylhydrazine and the toxic varieties of mushrooms.

The Diagnosis and Treatment of Insulomas. If it were possible to diagnose an islet cell adenoma or carcinoma before operation there would be no need for trying the patient on a diet; because in such cases surgery will give almost certain relief unless delayed until the neoplasm has advanced to the stage when metastases make the case an inoperable one. One of the most brilliant chapters in American surgery will be written when the results of operations on the pancreas for islet cell tumors have been recorded.

Unfortunately no one as yet has established the criteria necessary for diagnosing insulomas. Gammon and Tennery summarize what is known regarding the differentiation between hyperinsulinism resulting from the neoplasms of the islands of Langerhans and the manifestations from functional insulogenic hypoglycemia, as follows: "All that can be said is that there is perhaps a tendency for the disease (hyperinsulinism) to be more rapid in its development, more severe in its manifestations, more erratic in behavior and more likely to cause death when tumor is present than in functional hypertrophy of the islands."

If an exploratory operation on a patient suffering from hyperinsulinism reveals an adenoma, or carcinoma, of the body or tail of the pancreas it should be removed, if possible. In one of Evarts Graham's series an islet adenoma the size of a baseball was removed from a psychotic patient with a clinical cure for two years, without any present indication of recurrence. If there are metastases in the liver and extensive involvement of the surrounding structures the case is inoperable.

In making an exploration for an adenoma of the pancreas it should be remembered that some of those found have been quite small, yet their removal completely cured the patients of hypoglycemic symptoms. Smith and Seibel found at autopsy an adenoma in the head of the pancreas less than 1 cm. in diameter, yet the patient died in hypoglycemic coma. It therefore should be remembered that even an exploratory operation may not reveal the adenoma that is causing severe hypoglycemic symptoms.

It should not be forgotten that though adenomas of the islands of Langerhans are usually single, two or more may be found in the same patient, and the removal of one may not relieve the patient of his symptoms. Evarts Graham in one case operated on a patient who had severe hypoglycemic symptoms and he removed an adenoma from the anterior surface of the body of the pancreas. The symptoms continued unabated. Later the second operation by Graham revealed another adenoma on the posterior surface of the body of the pancreas. The removal of the second tumor relieved the symptoms.

Resections of the Pancreas in Hyperinsulinism. If an exploratory laparotomy on a patient suffering from hyperinsulinism does not reveal an adenoma or other operative lesions, but a normal appearing pancreas, should a resection be performed? As yet there are no criteria for performing resections of the pancreas in hyperinsulinism. Each case will have to be considered from its various aspects before deciding to resect a major part of the pancreas, or to close up the abdomen and give the patient another chance at dieting.

A brief review of some of the reported cases may provide data that should be helpful to the surgeon in making his decision in such a case.

The first resection of the pancreas for hyperinsulinism was performed in 1928 by Finney and Finney, who removed about three-fourths of the pancreas from a psychotic patient referred to them by Barker and Sprunt.

There was definite improvement, but not complete relief, though the blood sugar levels were higher following the operation. Six years later this patient committed suicide.

The next resection of the pancreas for hyperinsulinism was performed by Holman, with temporary relief of symptoms. This case was subsequently explored by Judd, who resected another portion of the pancreas with some relief, but the symptoms recurred.

Experience with Eight Cases of Surgical Hyperinsulinism. I have advised surgical intervention in seven cases of hyperinsulinism. In three cases resections of from one-half to five-sixths of islet bearing tissue of the pancreas resulted in clinical cures. In two cases of epilepsy associated with hypoglycemia resection was followed by slight improvement; and in one case in which there was a history of probable dyspituitarism resection of five-sixths of the pancreas failed to control the epileptic attacks or the hypoglycemia. In the seventh case the abdomen was closed without resection of the pancreas after an exploratory laparotomy which revealed a normal appearing pancreas. This patient since the operation has adhered more rigidly to his diet and has shown a lessened frequency of his attacks of convulsions. The eighth case in which I advised operation was a patient of Dr. J. E. Beck and Dr. G. O. Segrist of Mobile. They had made a diagnosis of hyperinsulinism from very low blood sugar readings in a man who had been incapacitated for work for a year or more because of recurring periods of unconsciousness. The patient was violently psychotic at times. On account of the severity of the symptoms a tumor was suspected and I advised that the patient be sent to Dr. Evarts Graham of St. Louis, who operated, removing a large islet tumor. The patient made a complete recovery. He has had no symptoms in two years and is working regularly.

Conclusions

1. Hyperinsulinism, or spontaneous hypoglycemia, is a frequent and widespread disease, numerous cases having been reported by discriminating clinicians in many countries.

2. The manifestations of hyperinsulinism are protean, and identical with the symptoms that have been reported from overdoses of insulin in the treatment of diabetes mellitus.

3. The anamnesis is important in making the diagnosis of hyperinsulinism in the mild cases. Usually, there is a history of attacks of weakness, nervousness, trembling and sweating before breakfast, one or two hours before noon and evening meals, before retiring and often during the night. The attacks are relieved by taking food. In the more severe cases in addition to the mild symptoms, there is a history of recurring attacks of unconsciousness and convulsions, or hysteria. Neuropsychiatric, gastrointestinal and cardiac symptoms may be pronounced.

4. Low blood sugar readings, before breakfast, one or two hours before meals and in attacks, and the occurrence of a hypoglycemic phase in dextrose tolerance tests, are necessary for proof that the symptoms are due to spontaneous hypoglycemia. Dextrose tolerance tests should be carried out for six full hours before excluding the diagnosis of hyperinsulinism. The symptoms may, or may not be, reproduced in the hypoglycemic phase of dextrose tolerance tests.

5. The secretory interrelations of the pituitary, thyroid and adrenal glands with the insular apparatus of the pancreas should be considered carefully before making a diagnosis of uncomplicated hyperinsulinism. Likewise, hypoglycemia from deficient glycogenesis should be excluded before making a diagnosis of hyperinsulinism.

6. The great majority of cases may be relieved by a moderately low carbohydrate, high fat diet with frequent feedings between meals, and at night if there are nocturnal symptoms. The diet should be prescribed to meet the individual needs of the patient under treatment.

7. Surgery offers relief in cases that cannot be relieved by properly directed and carefully carried out dieting over a period of a few weeks or months. The removal of insulomas, either adenomas or carcinomas, of the islands of Langerhans has resulted in clinical cures. Resection of the pancreas relieved the symptoms in about 50 per cent of reported cases.

8. Two fatal cases of islet cell carcinomas have been reported which were inoperable because of the size of the tumors and the presence of liver metastases. It, therefore, is important to make the diagnosis of hyperinsulinism early before the neoplasm of the islands of Langerhans has progressed to the inoperable stage.

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MASSIVE DOSES OF VITAMIN D IN THE TREATMENT OF PROLIFERATIVE ARTHRITIS *

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Recent interest in the treatment of arthritis, by massive doses of vitamin D,[1] has been sufficiently great to warrant a clinical trial of this mode of therapy in a group of patients with the chronic proliferative (infectious) type. Past experience of disappointing results when such recommended therapeutic agents as gold and sulphur were used over an adequately long period under controlled clinical conditions had rendered us somewhat skeptical but it appeared worthwhile, however, to determine if vitamin D might constitute a valuable adjunct to a composite program of treatment in this group of diseases.

Thirty-eight patients having chronic infectious or proliferative arthritis and two patients in the same group, but with histories of earlier rheumatic fever, were selected. These patients had been under observation for at least six months and six complete clinical and laboratory check-ups had been made. It was possible thereby to contrast their progress before and after the administration of large doses of vitamin D. In evaluating any therapeutic agent in the treatment of arthritis, such a control is more valuable than is a study of parallel groups (one with and one without the test treatment). Comparison before and after institution of the use of a given therapeutic agent in well-studied patients is of greater value in our experience than the analysis of data from treated and non-treated groups.

The indications for the use of massive doses of vitamin D are considered to be the presence of proliferative arthritis and, inasmuch as the work was experimental, no special selection was employed among members of this group, other than that any patient was eliminated whose general condition was such that a severe reaction might be disastrous.

Later, it became evident that the presence of a very sensitive colon contraindicated the use of the vitamin in large quantities. In general it was found that the type of arthritic patient for whom vaccine is indicated, that is, a patient in whom desensitization seems to be the main problem, was decidedly not the type in which to use massive doses of vitamin D. When a high sedimentation and low agglutination titers were taken to indicate the desirability of the employment of streptococcus vaccine, then the use of massive doses of vitamin D seemed inadvisable.

The method employed in this work had as its first step the evaluation of clinical progress and laboratory changes in each patient up to the time of administration of vitamin D. After this base line in degree of progress for

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six months was established massive doses of vitamin D with supplementary medication (vitamin B and calcium) were instituted and similar studies of the patient continued to see if more definite progress toward recovery would result.

The dose employed was never increased over 300,000 units of vitamin D daily and the ordinary dose most often used was 200,000 units daily. Under no circumstances did we see reason to increase the dose to the enormously high levels that have been reported by some workers.

The sources of vitamin D were as follows: irradiated ergosterol in sesame oil supplied for experimental purposes by the National Institute of Nutrition, Los Angeles; viosterol and vitamin D in propylene glycol.

The supplementary medication employed consisted of a good source of vitamin B, such as wheat germ or brewer's yeast and calcium supplied in the form of dicalcium phosphate and milk.

The additional treatment of these patients consisted of a definite regimen used in this Clinic. This treatment may be briefly summarized: Adequate rest, physiotherapy, heliotherapy, dietotherapy, treatment or early removal of foci, blood transfusions, orthopedic measures and intravenous bacterial antigen. Obviously, under such a program, there were individual variations. However, these were minimized as much as possible.

The results of treatment in 40 patients were evaluated in two ways. First, clinical improvement, such as diminution in joint pain, swelling and stiffness, increase in general strength, appetite and weight, was noted; second, laboratory changes were studied once a month and included the determination of the sedimentation rate, agglutination reactions for streptococci, morphological blood picture and the level of calcium and phosphorus content of the serum.

The percentage of clinical improvement noted was considered definite and clear-cut in 20 per cent; i.e., in eight patients in this series we could detect a definite progressive increase in appetite, weight, general feeling of strength and a decrease in joint swelling, pain and stiffness. Similarly, in eight patients, or 20 per cent of the total series, it was necessary to abandon the treatment entirely on account of unfavorable reactions.

One patient complained of violent persistent nausea for four days, intense headache and profuse sweating. In another patient, severe diarrhea was the only evidence of a reaction, but necessitated the withdrawal of the therapeutic agent. Reactions in the remaining six were vague conditions developing in the first week of treatment characterized by beginning loss of appetite, drowsiness, slight headache often present on awaking in the morning but worse with the advance of day. However, the symptoms in the latter disappeared in about 48 hours following the stopping of vitamin D.

The remaining 60 per cent, or 24 patients out of the 40 treated, during the period of our observation, showed no definite benefits that could be attributed to vitamin D therapy.

In more than half of the patients, therefore, vitamin D concentrates did not seem to hasten recovery. It should be borne in mind in this connection, however, that treatment problems in chronic proliferative arthritis are so complicated and so manifold in their aspects that we are hesitant to say at the present time that some of these 24 patients, during the next few months, may not show some improvement due in part to their vitamin D therapy.

From a study of over 500 cases the base line for the laboratory changes in patients under treatment in this Clinic is well established and in this series studied with the use of vitamin D no significant departure was observed. For example, the morphological blood picture did not alter in these patients more rapidly or more distinctly in general than it does in other patients being treated without vitamin D. Calcium and phosphorus determinations exhibited only minimal changes, the average increase in calcium content of the serum being 0.75 to 0.95 mg. All determinations were within normal limits. There was no significant change in the calcium phosphorus ratio noted.

These results may be briefly summarized as follows: On a composite program of therapy 40 patients with chronic proliferative arthritis received massive doses of vitamin D. Out of this group eight were definitely improved clinically, eight exhibited more or less severe reactions, the remainder exhibited no improvement attributable to the medication. The laboratory tests employed to follow the progress of these cases did not show any significant changes.

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CASE REPORTS

ARTHRITIS PSORIATICA; REPORT OF A CASE*

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This case of psoriasis and destructive bone and joint changes is reported because the pathological process of the bones and joints is of an unusual character.

Case Report

M. G., housewife, 57, native born, of Irish extraction, was admitted to the Psychiatric Clinic of the Institute of Human Relations, December 26, 1934, with a history of psoriasis and of multiple joint involvement leading to mutilating deformities of the hands and feet—the skin and joint conditions having both begun about 20 years ago. The reason for admission to the Psychiatric Clinic was that the patient had a psychosis of three months' duration characterized by depression, agitation, suicidal tendencies, somatic and self-accusatory delusions, and auditory and visual hallucinations; this mental condition was diagnosed by the staff as one of agitated depression (involutional melancholia). After about three months she was transferred to the Norwich State Hospital, the mental condition unchanged. Prior to the onset of the psychosis the patient had been considered a normal individual and had made a satisfactory adjustment to the environment in the face of a chronic and serious physical handicap.

Family History: The paternal grandmother died at the age of 92, of "arthritis." Beyond the fact that she had been unable to walk for 10 years prior to her death, no details were obtained concerning the nature of the supposed arthritis. The family history shows no other instances of rheumatic disease and is non-contributory in other respects.

Past History: The birth and early development are considered to have been normal. The patient was married at the age of 26 (1903) and widowed 12 years later. There were three pregnancies (1904, 1908, and 1911), all going to term. The menopause occurred about 1924 and was associated with the appearance of black spots before the eyes. Her general health up to the age of 37 (when the present illness began) was good, but there was some tendency to obesity. The past infectious illnesses include grippe (two attacks), and possibly measles and chicken pox. Although the patient is said to have suffered from "valvular disease" of the heart since about the time of onset of the present (physical) illness, there have been no definite symptoms of heart failure. A review of the organ systems discloses the following: chronic constipation; some tendency to gaseous eructations and "sour mouth"; occasional mild swelling of the feet (probably postural or due to local lesions rather than cardiac); occasional frontal headaches; vague history of precordial pain about three years ago. There is no history of tuberculosis, syphilis, or gonorrhea.

Present Illness: About 1913 (age approximately 37) the patient developed a psoriatic rash and at about the same time some form of multiple joint involvement

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that suggested at the time a questionable diagnosis of rheumatic fever. She remained in bed for about a year, during which time all her teeth gradually dropped out. The rash was early generalized, remained permanent and was refractive to treatment; however, it usually receded during the summer months of July and August. The joint involvement likewise persisted permanently; and it included the elbows, knees, and the articulations of the hands and feet. Deformities of the hands and feet appeared early in the course of the disease and progressed steadily, reaching in 1929 practically the extreme stage noted at the time of admission. Apart from the first year of illness, the patient was up and about, and active in caring for a large household until incapacitated by the psychosis.

General Physical Examination: The patient was short, of pyknic habitus, and despite the history of loss of weight, appeared well developed and nourished. Facial hirsuties and a tendency to prognathism were apparent; otherwise there were no signs related to possible endocrine stigmatization. A slight degree of exophthalmos (constitutional) was noted. The irides were discolored (old iritis); both eyes showed posterior synechiae; and the left eye was highly myopic with a posterior crescent. All the teeth were missing and the alveolar processes absorbed. The breasts were atrophic. The heart did not appear enlarged on percussion; the sounds were regular and of good quality, with accentuation of the second aortic sound and with a systolic murmur at the apical region. The radial artery was compressed with difficulty; and the blood pressure was 174 systolic and 100 diastolic. A second degree rectocele and external hemorrhoids were present. There was no evidence of trophic disturbances of the skin in the extremities and the dorsalis pedis was easily palpated in each foot. The neurological examination was negative: there was no motor weakness except that due to the bone and joint involvement; the deep reflexes were active and equal, and sensory changes in the extremities were not elicited.

Examination of the Skin: There was a generalized psoriatic eruption with free coalescence of lesions and the production of many gyrate and polycyclic forms. The nails of the hands and feet were thickened, crusted and lined with prominent transverse grooves. The palms of the hands alone were spared in the generalized involvement.

Orthopedic Examination: There was evidence of multiple joint involvement with the most striking changes in the distal portions of the extremities. The spine showed a moderate degree of kyphosis in the dorsal region and its motility was generally reduced.

Both shoulder joints appeared to be of normal size and permitted free movement except that on the right the patient could not raise the arm above the horizontal level and had to flex the elbow to reach overhead. The right elbow joint (figure 1) was enlarged and permitted extension only to about 120 degrees; the size of the left elbow joint and its movements were not remarkable. Pronation-supination of the forearm was considerably limited on the right but quite free on the left. There was complete ankylosis of the right wrist and partial of the left.

Both hands (figure 1) were deformed and shrunken to at least half their normal size, giving one the first impression of a congenital anomaly. The skin over the dorsum of the hand, particularly over the fingers, was loose, with the formation of transverse grooves most marked at the metacarpal-phalangeal joints. The interphalangeal joints showed complete ankylosis while the metacarpal-phalangeal articulations were transformed into ball and socket joints. There was practically no power in the fingers, the patient holding objects by pressure at the palms.

Motion was free and power good at the hip joints, which presented no superficial signs of abnormality. The right knee was slightly increased in size but permitted free motion; the left knee gave no positive findings. Movements of flexion-extension at both ankle joints were limited to within a range of about 10 degrees.

At both sub-astragaloid joints the movements of inversion-eversion were practically nil. The feet (figure 2) showed changes corresponding to those in the hands: considerable shortening at the metatarsal regions; marked shrinkage and deformity of the toes; complete ankylosis of the interphalangeal joints; transformation of the metatarsal-phalangeal joints into ball and socket articulations; and practically com-

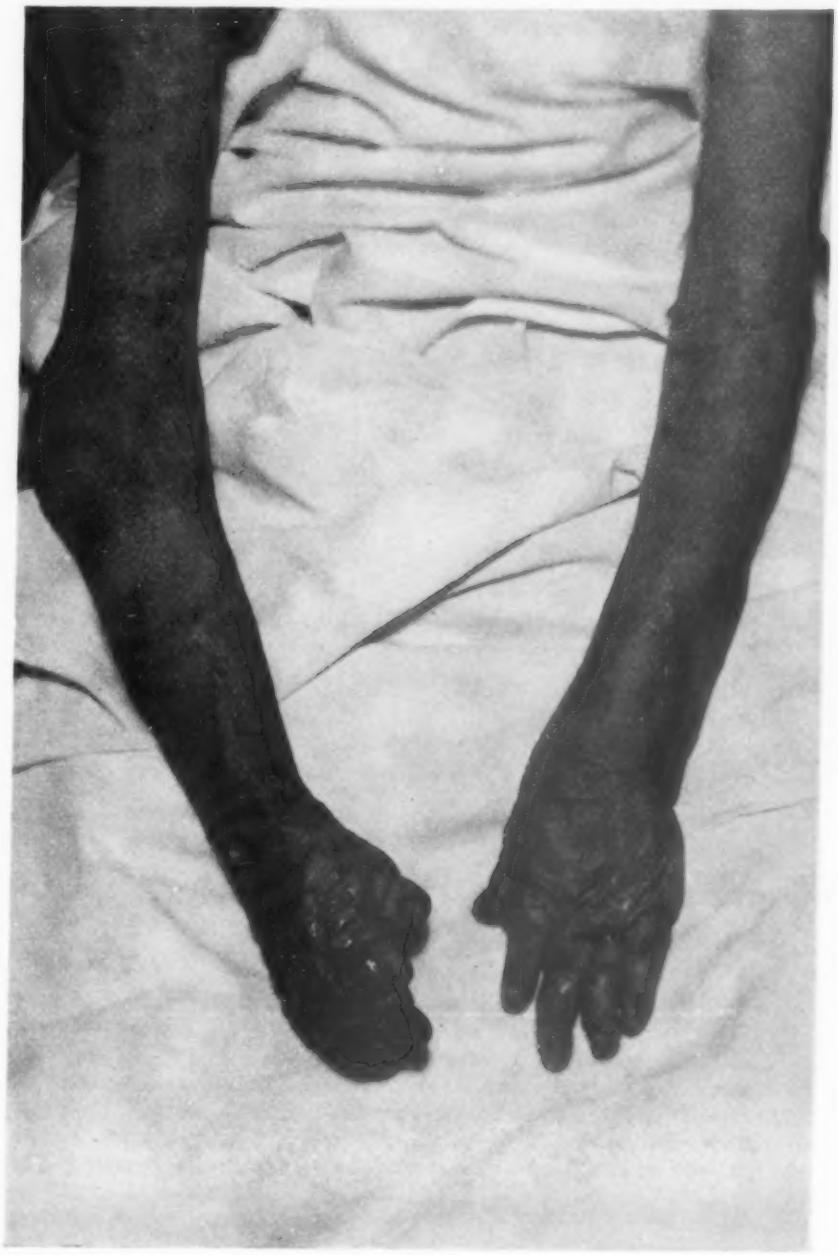

FIG. 1.

plete loss of power in movements of the toes. As a result of the deformities in the feet, the patient walked on the outside of the left foot and mostly on the heel of the right with a shuffling gait.

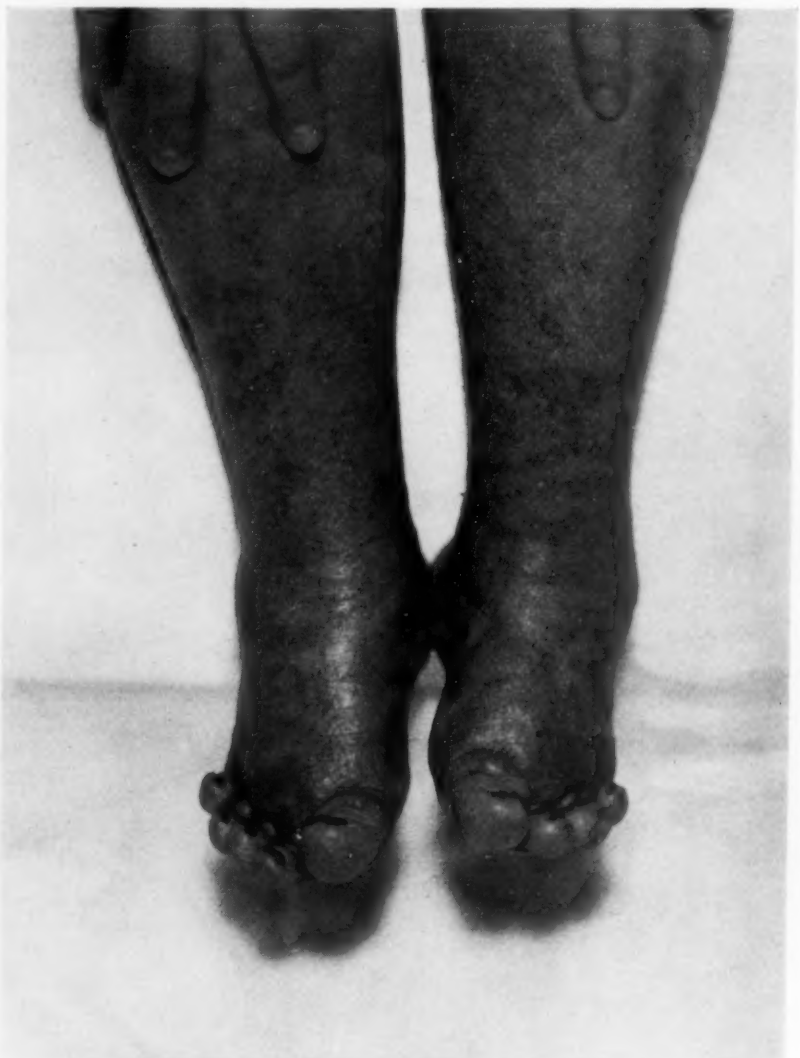

FIG. 2.

Laboratory Data: Blood examination showed 3,700,000 red blood cells per cubic millimeter with 70 per cent hemoglobin (Sahli); and 7,500 white blood cells with a normal differential count.

Routine urine examination was negative except for the presence of 2 to 4 finely granular casts per low power field.

The blood Kahn test was negative. Examination of the spinal fluid gave normal results with regard to hydrodynamics, chemistry, cell count, and the Wassermann and colloidal gold tests.

Blood chemistry (January 14, 1934) showed the following:

Serum total proteins 7.61 per cent
" albumin 4.11 per cent
" globulin 3.50 per cent
" calcium 8.74 per cent
" phosphorus 4.01 per cent

A hemolytic streptococcus agglutination test (November 24, 1935 *) in which the patient's serum in dilutions ranging from 1 : 10 to 1 : 1280 was tested with a strain of hemolytic streptococci known to be agglutinated by arthritic serum in high dilution, was entirely negative.

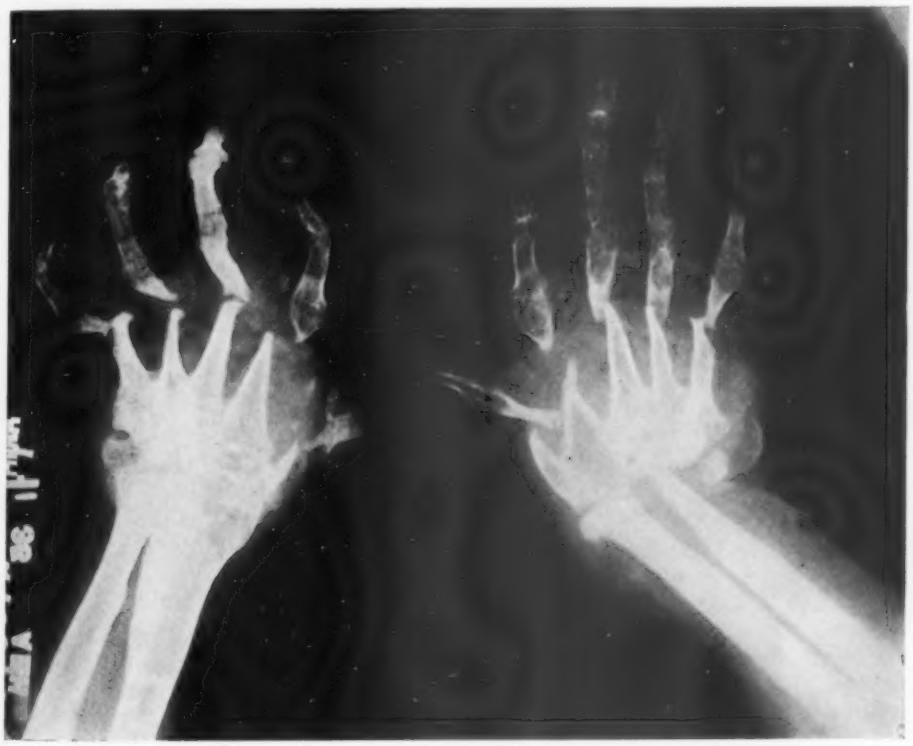

FIG. 3.

Radiographic Report (Dr. H. M. Wilson. Yale University School of Medicine): Films of both hands (figures 3 and 4) and the left foot (figures 5 and 6) made in this laboratory, and of the shoulders, knees and elbows made in another laboratory (Norwich State Hospital †) reveal the most striking changes in the extreme distal ends of the extremities with similar but milder changes in the more proximal portions of the extremities. There is some osteoporosis of all the bones, characterized by concentric atrophy with evidence of thinning of the cortical compact bone and associated with some coarsening of the trabeculations, which reaches an extreme degree in the

* This test was carried out in the bacteriological laboratory of the Hospital for Joint Diseases, New York City, through the courtesy of Dr. H. L. Jaffe.

† The coöperation of Dr. C. Waterman, Superintendent of the Norwich State Hospital, Conn., made possible the follow-up study of the patient and access to these films.

phalanges of the left hand. The tendency to osteoporosis becomes accentuated about the joints, especially in the distal ends of the extremities, where massive absorption of bony substance occurs.

There are osteochondritic changes in the shoulder joints, most marked in the left shoulder about the humeral head characterized by irregular and alternating areas

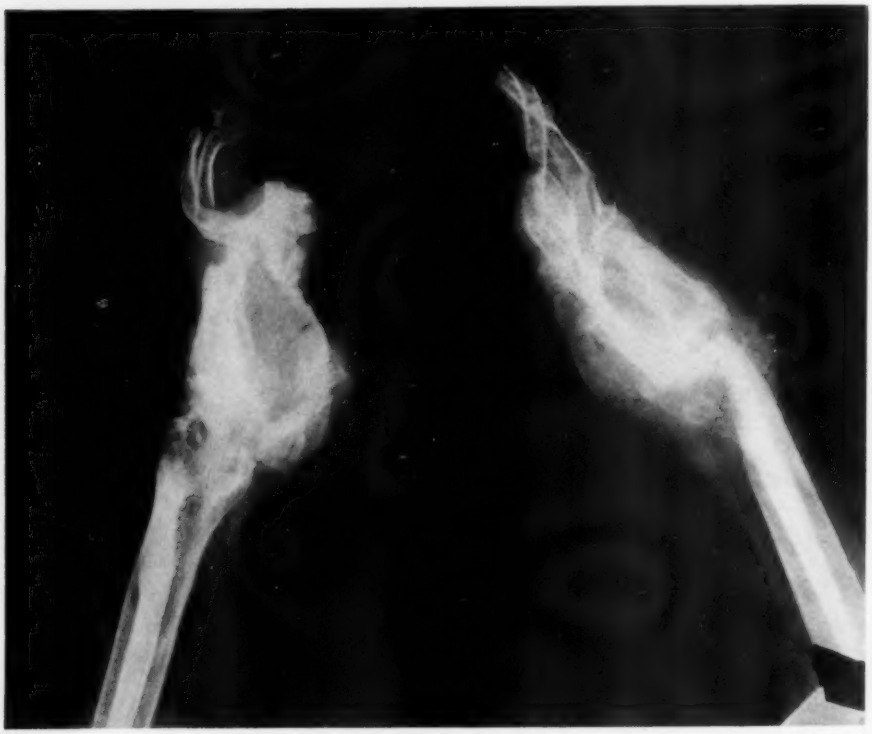

FIG. 4.

of rarefaction and condensation. The right shoulder girdle shows a tapered narrowing of the outer end of the clavicle with loss of substance from its distal extremity. The acromioclavicular joint space is widened. There is condensation and irregularity of the acromion process.

Moderate proliferative changes are noted in both knee joints, particularly about the superior aspects of the patellae. This change appears to be associated with localized decalcification along the superior border at the attachment of the quadriceps tendon.

The elbow joints show narrowed joint spaces with an irregular osteoporosis of the olecranon process giving it a spongy appearance. There appears to be flattening and possibly telescoping of the radial head on the right.

At the left hand the distal 2½ centimeters of the left ulna are tapered to a point, with sclerosis and obliteration of the medullary cavity; the lower 3 centimeters of the left radius likewise show sclerosis and obliteration of the medullary cavity but without the tapered narrowing, and the articular surface is deformed. The proximal carpal bones with the exception of the pisiform are missing while the distal carpal bones are fused into a contracted and flattened mass. The carpo-metacarpal joint spaces are obliterated and the metacarpals show the same tapered narrowing with

loss of the heads which characterized the change in the left ulna. The proximal portions of the proximal phalanges show essentially the same changes as do the metacarpals. The distal portions of the proximal phalanges and the remaining phalanges show extreme osteoporosis with cortical outlines a fraction of a millimeter in width. As a result of the loss of bony substance of the lower ends of the radius

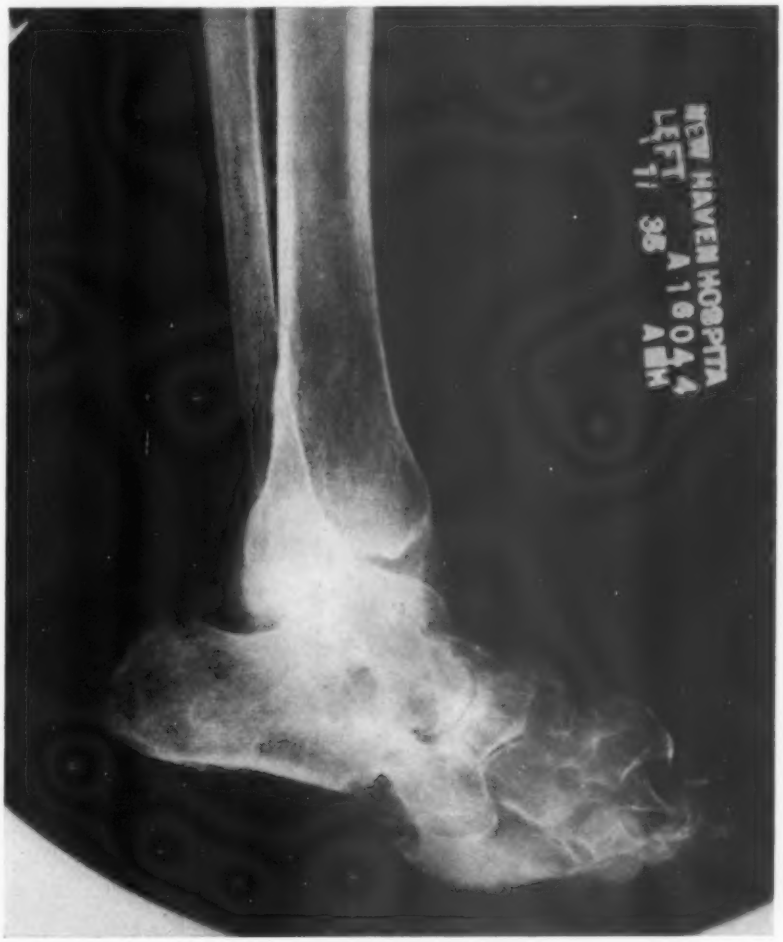

FIG. 5.

and ulna, and of the carpals, metacarpals and phalanges, there is extreme shortening of the hand with the soft tissues creased and redundant. An essentially similar process involves the right hand although the changes are somewhat more pronounced in the hand and less marked in the carpus and radio-carpal joint than noted on the left.

The tarsals, metatarsals and phalanges of the left foot show a process similar to that involving the corresponding bones of the hand.

Comment

The clinical association of psoriasis and joint involvement, first comprehensively studied by Bourdillon (1888),[1] has been frequently described in the recent literature. Although practically every type of chronic joint disease has

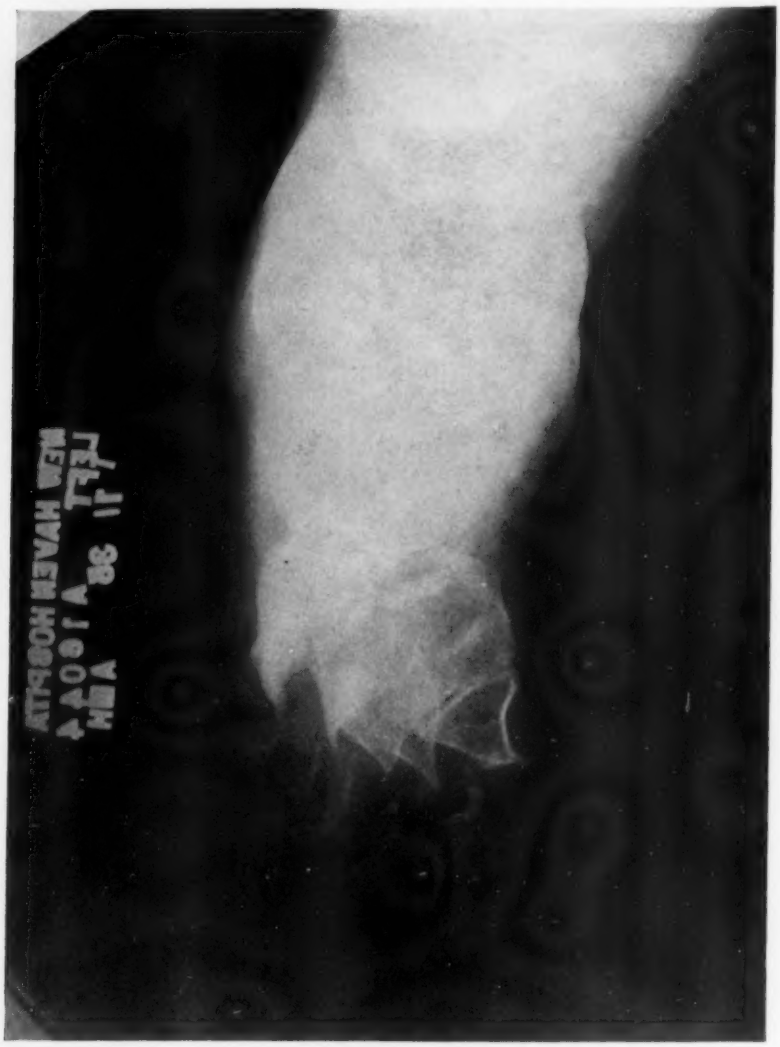

Fig. 6.

been reported as occurring with psoriasis, one variety has received special emphasis with regard to its relationship to the skin condition. This form of arthritic disease is characterized by chronic usually multiple joint involvement often leading to early deformity and to gradual destruction of the joints. Some authors (Adrian,[2] Nobl and Remenovsky,[3] Zellner [4]), on the basis of certain clinical and roentgenological criteria, consider this type of arthritic disease peculiar to psori-

asis and would restrict the term "arthritis psoriatica" ("psoriasis arthropathica") to cases of psoriasis with this form of joint involvement. Others (Bauer and Vogl [5]), on the other hand, although admitting the existence of a probable etiological relationship between psoriasis and joint disease, deny the specificity of the articular changes of arthritis psoriatica and place them in the category of ordinary primary chronic (infectious) polyarthritis.

Whatever its nosological status, the group of cases included under the heading of arthritis psoriatica are characterized, as indicated above, by the frequent tendency to marked destructive changes of the joints. In some cases the destructive process also involves to a considerable degree the bone in the distal end of the extremities, resulting in a picture that would appear to be a mild form of the involvement characteristic of our case. Thus cases with atrophy and destruction of the phalanges of the hands and feet to the extent that several phalanges have been almost entirely absorbed are not uncommon (Adrian,[2] Wollenberg,[6] Balzer and Burnier,[7] Ström,[8] Schumacher and Lauter,[9] Nobl and Remenovsky,[3] Scholl,[10] Rodner [11]). Extension of the destructive process to the metacarpals and carpals has also been observed, if less frequently (Falk,[12] Zellner [4]). Furthermore in one case with metacarpal involvement (Zellner [4]) the distal ends of these bones have disappeared leaving tapering fragments of bone as seen in our case.

The involvement of the bone in the proximal portions of the extremities has not been described as frequently in arthritis psoriatica; but in a case reported by Lotze [13] an area of rarefaction and condensation in the head of the humerus, and an area of absorption in the patella associated with proliferative changes in the knee joints resemble the lesions of the corresponding areas in our case.

In reviewing the literature we were able to find the description of only one case of psoriasis and bone and joint involvement which we would consider comparable to ours with regard to severity as well as to type of bone and joint change —that presented by Bauer and Vogl.[5] In comparing the two cases one notes similar clinical courses and the same type of involvement of the hands and feet as characterized by the extensive loss of bony substance and the tapered narrowing of bony fragments. Bauer and Vogl consider their case an instance of ordinary primary chronic (infectious) polyarthritis, in keeping with their view, referred to above, that cases of arthritis psoriatica fall into that category.

The bone and joint changes of our case also suggest a comparison with those described in a condition independent of psoriasis; namely, a rare form of arthritis, "main en lorgnette," only two cases of which have been reported in the literature: the original by Marie and Léri,[14] and the second by Weigeldt.[15] These cases resemble ours in showing the following features: chronic progressive multiple joint involvement with extreme changes in the distal ends of the extremities; massive absorption of bone in the hands with tendency to tapered narrowing of bony fragments; and formation of transverse folds in the skin of the fingers (due to the disproportionate shrinkage of the bones and the soft tissues). This peculiar folding of the skin of the fingers, suggesting the appearance of an opera glass, prompted Marie and Léri to select the descriptive name of "main en lorgnette." The two cases designated by this name are considered by their respective authors as special instances of chronic infectious polyarthritis.

The fact that a bone and joint process similar to that in our case appears in a condition not associated with psoriasis would argue against the assumption that

the type of bone and joint involvement characteristic of our case is peculiar to the skin condition, even if the two may be etiologically related.

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CONGENITAL DILATATION OF THE PULMONARY ARTERIES REVEALED BY ROENTGENKYMOGRAPHY *

By Sydney E. Johnson, M.D., F.A.C.P., *Louisville, Kentucky*

Roentgenkymography is so new an addition to the diagnostic procedures of roentgenology that few physicians in general practice are aware of its value and diagnostic indications. The writer is of the opinion that the method has a wide field of usefulness and that it will come into general use in radiological practice as soon as its various applications are more generally known.

Roentgenkymography differs from other roentgenographic methods in that its single function is to record movement (and negatively, the absence of movement in organs or parts of the body that normally have movement). With this method it is possible to make a permanent graphic record of the movement of any part or organ of the body that can be depicted in the ordinary roentgenogram. Often the movement curves are susceptible of quantitative and qualitative analysis of great accuracy. Ventricular, auricular, and arterial movement curves are characteristic and show characteristic modifications in certain cardiovascular diseases. Movements of the diaphragm, gastrointestinal canal, deglutition, articulations, chest wall, etc., may be studied in the fixed curves of

* Received for publication April 23, 1936.

the kymogram, or the recorded cycle of movement may be reproduced visually in a special viewing machine, the kymetoscope, which produces the illusion of continuous motion.

The mechanical details and groundwork of roentgenkymography have been covered by Stumpf,[1] and Hirsch.[2] The next logical step is the reporting of specific cases in which the method has elucidated otherwise obscure points in the diagnostic picture. To justify itself, the method must give information that is not as readily obtainable by other methods. A first case of this kind was reported by the author in August 1935.[3] The case reported herewith furnishes another illustration of the value of roentgenkymography in a type of case that usually presents diagnostic difficulties, congenital heart disease.

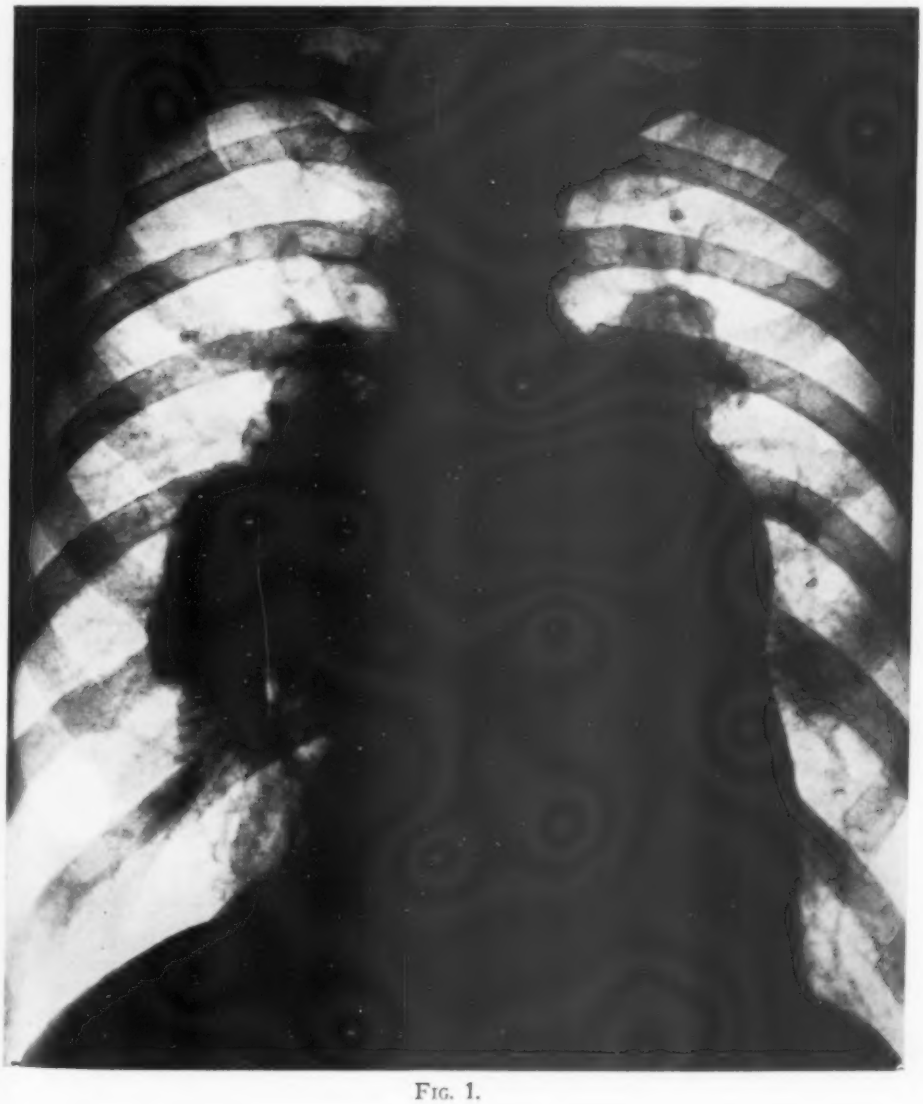

FIG. 1.

Case Report

The subject of this report is a white male school teacher, aged 38 years. He has no complaint and was unaware of his abnormality until he applied for life insurance in December 1934. His mother died in 1909, probably of tuberculosis. Aside from this, the family history is negative. He has been in good health prac-

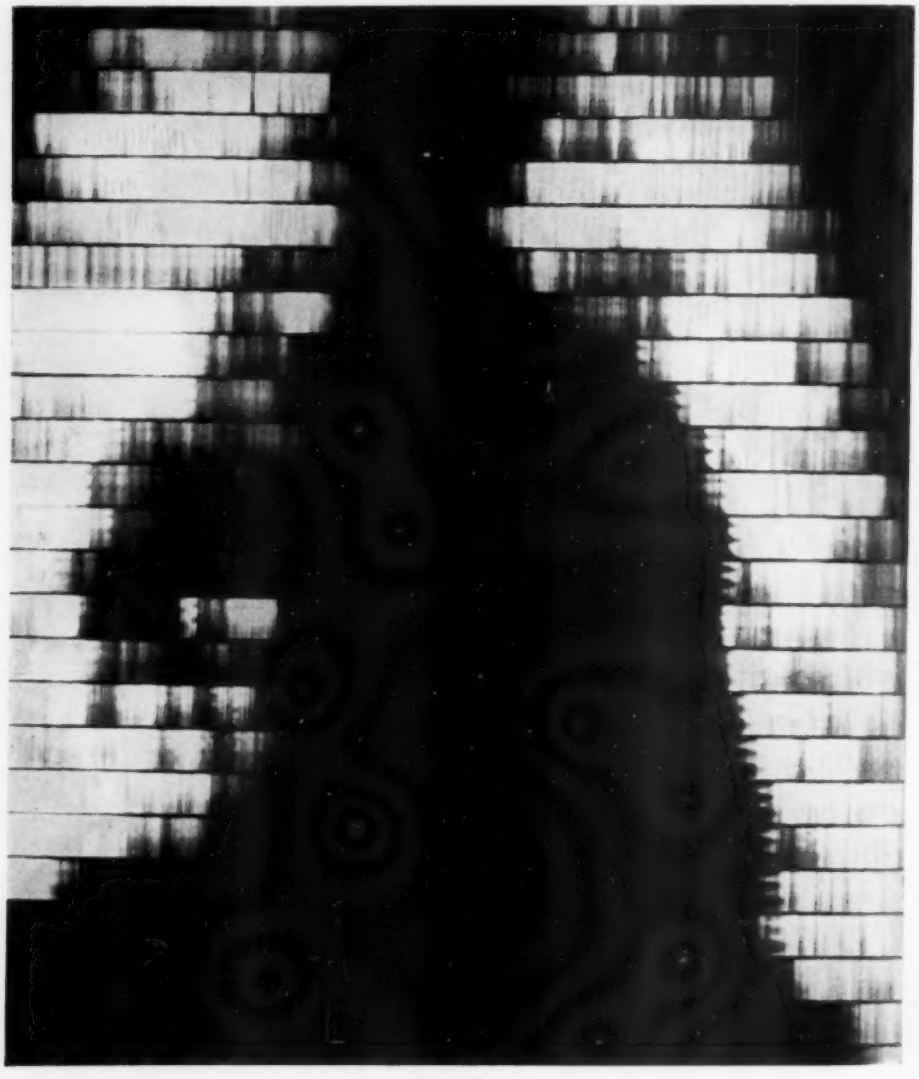

Fig. 2.

tically all of his life, but says that when he was a child his parents were told that he had an abnormal heart. He led a life of normal activity. There is no history of cough or expectoration. The man shows average build, development and nutrition. Pulse rate 84, blood pressure 104 systolic and 78 diastolic, respiratory rate 20, normal

temperature. He served in the World War and was discharged without disability. His tonsils were removed in 1929, and the appendix in 1930. In 1927 he had influenza and, due to a rather prolonged convalescence, visited a large clinic for general medical examination. He was told that he had mitral stenosis and would have about 20 per cent disability.

In 1934 an insurance company's medical examiner elicited percussion findings which led him to suspect old fibrotic tuberculosis and the applicant was referred to the Waverly Hills Tuberculosis Clinic. A chest film made at the Clinic (figure 1) shows large, sharply defined masses projecting into both lung fields, and pronounced enlargement of the upper left cardiac border. The lungs are singularly clear. No evidence of tuberculosis was found. The differential diagnosis lay between Hodgkin's disease or some other type of neoplasm and anomalies of the heart and great vessels. A faint presystolic murmur was the only abnormal heart sound elicited. There was no clubbing of the fingers. No subjective symptoms were present.

Because of the unusual roentgenographic findings, the patient was referred to the writer for roentgenkymographic examination with the idea of determining whether the masses in the thorax were of vascular origin or solid tumors. This question is clearly answered by the kymogram (figure 2). Not only do the masses show expansile pulsation, but the curves are unmistakably arterial.

In the light of these findings and of the history we believe that the evidence is sufficient to justify a diagnosis of congenital dilatation of the pulmonary arterial trunks and probably the ductus arteriosus and conus arteriosus. Conventional teaching would lead us to anticipate more in the way of physical signs and subjective symptoms in cases of this type. It seems probable that roentgenkymography will teach us some hitherto unknown facts about these cases, especially in relation to clinical manifestations.

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RAYNAUD'S DISEASE IN MAN *

By A. M. Rechtman, M.D., F.A.C.S., *Philadelphia, Pennsylvania*

Raynaud's disease in man is not common. Only seven cases were seen at the Mayo Clinic [1] which fulfilled the criteria Allen and Brown considered necessary for a diagnosis. It is generally conceded that the majority of male patients in whom a diagnosis of Raynaud's disease has been made have in reality been cases of thromboangiitis obliterans.

Raynaud described four features whose presence he considered necessary for a diagnosis of the disease bearing his name.

1. Episodes of change in color, of the vasospastic type, excited by cold or emotion.

* Received for publication January 2, 1935.

2. Bilaterality.
3. Presence of normal pulsations in the palpable arteries.
4. Absence of gangrene or its limitation to minimal grades of cutaneous gangrene.

To these Allen and Brown [1] added two further criteria.

5. The absence of any disease which might be causal, such as organic disease of the nervous system.
6. Symptoms of two years' or longer duration.

The author feels that the following further requirements should be insisted upon in the interest of more accurate differential diagnosis.

7. Obliterative vascular disease should be excluded, not only by the absence of gangrene (or its limitation to minimal cutaneous areas), but also by the determination of normal arterial pulsations by Pachon oscillometric readings, and by the demonstration of normal reflex temperature variations in the affected limbs with the thermocouple.
8. The characteristic changes in the capillaries of the nailfold, described by Brown,[2,3] should be shown to be present.

Two male cases of peripheral vascular disturbance are presented which conform to the above criteria for Raynaud's disease. Both were studied on the author's orthopedic service at the Jewish Hospital in Philadelphia.

Case Reports

Case 1. M. K., male, aged 36. The patient's symptoms started six (**6**) * years before his first visit on January 24, 1932. When his hands were exposed to cold weather, the second, third, fourth and fifth fingers became numb and "absolutely white." (**1**) The two distal phalanges of the second and third fingers, the distal phalanx of the fourth finger and the tip of the fifth finger of the right hand were involved. The numbness would abate when the patient was in a warm room for 30 minutes, or within five minutes if the hand was placed in hot water, when it then became red and dusky. Hyperesthesia as a pin- and needle-like sensation and a "scratchy, irritating, queer feeling" persisted until the normal appearance was restored. Placing the hands in cold water for five minutes caused the color changes. He learned to protect his hands against the cold which caused the syndrome and to warm them to hasten recovery.

On examination, January 30, 1932, at a room temperature of 70° F. the color of both hands (**2**) was red and dusky, to above the wrists. The left or subjectively uninvolved side was more dusky. The face had the same color changes, but not the remainder of the body. Elevating the hands lessened the color, but not to the normal. The pulsations (**3**) were equal on both sides and of good volume in all the vessels of the upper extremities. The radial, and then the ulnar arteries were compressed, but no occlusion of the smaller vessels was demonstrated.

Pachon oscillometric (**7**) studies of the extremities showed the following readings:

Right Arm	4	Left Arm	5
" Forearm	8	" Forearm	6
" Foot	2	" Foot	1
" Ankle	5	" Ankle	5
" Calf	10	" Calf	10

* The bold face numbers coincide with those of the criteria previously recorded as necessary for a diagnosis of Raynaud's disease.

Thermocouple (7) readings (Coller and Maddock) were taken. The patient was exposed for an hour; the room temperature was 70 degrees. The average temperature on the right side was 28 degrees C. and on the left side 28.5 degrees C. The body was wrapped in a rubber sheet, surrounded by blankets for an hour and the skin temperature readings were again determined. The right side averaged 32 degrees C. and the left side 32.4 degrees C.

The systolic blood pressure was 106. There were no evidences of trophic changes in the nails (4) or of gangrene. The family history was negative for circulatory disturbances.

Roentgen-ray examination (5) showed no evidence of a cervical rib or other cervical bony lesion to account for the disturbed circulatory condition. Examination of the capillaries (8) of the nailfold * showed the findings to be similar in the fingers of either side (2). The capillaries in the field were shorter and fewer than usual. The capillaries were tortuous and slightly more dilated than normal.

Discussion. This case fulfilled seven and partially the eighth criteria for a proved diagnosis of Raynaud's disease. The bilaterality was but partially fulfilled. The color syndrome with pallor was present in the right hand only. When no attack was present, the color of both hands was a dusky red. The capillary nailfold study showed findings on either side, similar to those seen in patients with Raynaud's disease.

Case 2. L. R. W., male, aged 22, was referred by Dr. A. E. Oliensis. History: The patient first noticed the condition four years before his examination on May 5, 1933. He said the second finger of the left hand was blanched (white) on change of weather. The color changes occurred in cold or warm weather on damp or mucky days; and they also occurred when he put his hands in cold water (1). He first had a numb and stiff feeling, the part became white and then changed to a slightly reddish hue and felt warmer than normal. This continued for about 10 minutes. The color variation occurred at times when he was very tired, or if he washed his hands briskly. Two years after the onset, the third and fourth fingers were similarly involved. The precipitating factors remained the same. At times both hands were affected (2). During six months previous to this examination the left hand was only occasionally involved and only in very cold weather. The right hand was usually involved.

The patient said he made a bid of 420 of spades in a pinochle game and needed eight points to win. Toward the end of the playing he noticed that the second, third and fifth fingers of the right hand were blanched and white. The fifth finger was but rarely involved and had been involved only for the preceding year. The fifth finger was involved about one time in 50 episodes of change of color as compared with the second and third fingers of the right hand. The second finger on the left hand was involved about one time in ten.

The more frequent involvement of the right hand may have been due to its greater use in shaking hands (4), i.e. by pressure; or by its use in holding objects, such as a glass of ice water. The right hand alone was involved when the patient was excited, as during a card game. The stimulation of exposure to cold, however, caused both hands to be affected.

Examination: The color of the patient's hands (1) changed from time to time during the several examinations made. The finger nails were all of a dusky hue. At times the color was normal. The color of the hands, to above the wrists, was usually duskier than normal. The color appeared normal when the hands were warmed beneath a blanket for an hour. At such times only were the hands warm.

* I wish to express thanks to Drs. Mitchell Rubin and C. H. Church of the staff of the Children's Hospital, Philadelphia, for their aid in the capillary nailfold studies.

The patient complained of a tingling sensation when the fingers were blanched. This continued during the period of cherry redness which followed. Blanching occurred on pressure of the hands, exposure to cold, and after excitement. It lasted for a period of from ten minutes to an hour and was of longer duration on a cold day. Blanching and stiffness first occurred in the second and third fingers and then in the fifth finger of the right hand. The color of the fingers changed to a dusky or purplish blue as the blanching abated. There was a sensation of numbness but no pain and the color gradually became a beefy red and a tingling sensation occurred. The natural color then returned but was a deeper red than normal unless the hands were warm. The normal color was slow in returning but it could be hastened by the application of heat or by massaging the fingers.

A study of the pulses (3) on palpation showed them to be equal in force and volume and present in all the palpable vessels of the extremities. Compression of the radial and then the ulnar arteries in both hands showed a normal return of the blood flow. The blood pressure was 114/80 on the left side and 112/82 on the right. Pachon (7) oscillometric readings were:

Right	Wrist	2	
"	Forearm	5	
"	Arm	5	
"	Foot	½	
"	Ankle	1¼	
"	Calf	7	
"	Thigh	6½	
Left	Wrist	1	
"	Forearm	4½	
"	Arm	4½	
"	Foot	+—	
"	Ankle	1½	
"	Calf	6	
"	Thigh	6	

Thermocouple (7) readings (Coller and Maddock) before dilation, at a room temperature of 72° F., showed the right hand averaged 23° C., and the left hand 23.4° C. After the patient was wrapped in a rubber sheet and surrounded with blankets for an hour the average skin temperature of the finger tips was 31.6° C. on the right side and 32.3° C. on the left side. There was no evidence of trophic, (4) gangrenous or ulcerative changes. Roentgen-ray examination for cervical rib was negative. A study of the capillaries (8) in the nailfold showed fewer capillaries to the field. The flow of blood in the capillary loops was slowed or stopped. The capillaries were more tortuous and had bulbous tips.

Discussion. This case fulfills all eight criteria herein recorded for a diagnosis of Raynaud's disease.

Summary

Two cases of Raynaud's disease in male patients are reported fulfilling the four criteria of Raynaud, and the two of Allen and Brown. These cases also met the additional diagnostic requirements suggested by the author; namely, normal oscillometric readings, normal reflex temperature variations, and characteristic abnormalities of the nailfold capillaries, in the affected extremities.

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EDITORIAL

THE GASTRITIS PROBLEM *

In the past decade there has been a marked revival of interest in gastritis. This is largely attributable to the following factors: (1) the present vogue, especially on the continent of Europe, of performing gastric resection for benign gastric and duodenal ulcers, as well as for malignant lesions, thus permitting histopathologic study of fairly large portions of the freshly resected gastric tissue; (2) the more general use of the gastroscope, which has been greatly improved in recent years; (3) progress in the roentgenographic study of the mucosal relief. Accessory to these major factors are the following: specialized biochemical and cytologic studies of the gastric secretion as an aid to the diagnosis of gastritis; researches directed to the experimental production of the lesion; investigations as to the rôle gastritis plays in the genesis of ulcer, carcinoma, various forms of anemia, and postoperative sequelae; accretions to knowledge from gastrophotographic observations; speculations concerning the clinical significance of gastritis when associated with duodenal or gastric ulcer, and finally, the influence of an increasing literature on the subject in the form of articles, monographs and atlases.

The problem of most concern to physicians and surgeons, simply stated, is this: To what extent is gastritis or gastro-enteritis, especially in its chronic form, the underlying cause of those conditions diagnosed as pseudo-ulcer, nervous indigestion, gastrotoxic hemorrhage, duodenitis, gastrogenic diarrhea, achylia gastrica, pseudocholecystitis, and of those relatively infrequent cases presenting antral defects, which are usually labeled scirrhous carcinoma or syphilis but which do not present evidence of either on histologic examination of the resected tissue? The same problem applies to certain late postoperative sequelae. What diagnostic procedure is the most reliable? Granting the presence of gastritis, to what extent is that condition responsible for the underlying complaint in a given case?

With certain primary and secondary types of gastritis—acute, subacute, chronic phlegmonous, specific and perianastomotic—we have long been familiar. The acute and chronic forms of alcoholic gastritis, atrophic gastritis associated with pernicious anemia, and the phlegmonous form of gastritis have been particularly well known. The hypertrophic, subacute and chronic forms have been frequently found at necropsy to be associated with disease of the liver, heart, gall-bladder and certain metabolic and endocrine disorders. Syphilitic gastritis in its various forms has been encountered repeatedly. In more recent years we have become impressed with the frequency of occurrence of hypertrophic, erosive and ulcerative forms of subacute gastritis in association with obstructive lesions of the stomach and duodenum. Baker's recent histopathologic studies of the

* Submitted for publication July 30, 1936.

gastric mucous membrane of patients undergoing gastric resection for malignant and benign lesions, with or without obstruction, also discloses the high frequency of occurrence of definite gastritis even in gastric mucous membrane remote from the lesion. This fact does not necessarily imply that gastritis was a precursor of the ulcer or cancer.

Of especial interest are those instances of primary gastritis encountered at operation and confirmed by histologic examination of excised or resected gastric tissue. In such cases the inflammatory process is sufficiently extensive to give rise to gross defects, usually antral in situation and recognizable by the ordinary roentgenologic technic. Such defects are indistinguishable from those produced by carcinoma in particular, by syphilis, by chronic hypertrophy of the pylorus, and by gastric ulcer when associated with antral spasm. From a symptomatic standpoint the cases can roughly be divided into three types according as to whether they simulate: (1) cases of ulcer or cancer with irregular symptoms, (2) cases in which the symptoms closely simulate those of ulcer, and (3) cases characterized by pain, or simulating cholecystic disease.

From the symptomatic standpoint, the traditional conception of gastritis, of the subacute and chronic variety in particular, in contrast to the contemporary conception, is worthy of consideration. Past teaching and experience led to the belief that changes confined to the gastric mucosa did not necessarily give rise to any frank gastric phenomena, with the exception of occasional hemorrhage and possibly of vague epigastric discomfort, although such indirect symptoms as anemia and intestinal disturbances, especially diarrhea, frequently occurred. But such authorities as Faber, Schindler, Henning, Konjetzny, Katsch and others, on the basis of gastroscopic, surgical and pathologic findings maintain that a variety of symptoms common to gross lesions of the stomach may be engendered by the various forms of gastritis. While it is still true that extensive gastritis may be present without giving rise to any appreciable gastric disturbances, increasing experience justifies the pronouncement of the authorities just cited. Certainly, primary subacute and chronic, erosive and ulcerative forms of gastritis, in which the gastric content contains free hydrochloric acid, do give rise to symptoms highly suggestive of gastroduodenal ulcer or to massive hemorrhage; and the chronic hypertrophic anacid variety may engender less active symptoms suggestive of cancer, cholecystic disease, or functional gastric disorders as well as of ulcer.

Of all the procedures advanced for the diagnosis of gastritis, it is generally conceded that gastroscopy is the most reliable. Careful roentgenoscopic study of the mucosal relief is helpful at times. In Berg's opinion, characteristic of gastritis from the roentgenologic standpoint, is the elevation, swelling, coarseness and stiffness of the mucosal fold, the product of inflammation. The atrophic, erosive, and superficial ulcerative forms are usually difficult of detection. An inflammatory condition following gastroenterostomy may be indicated by swelling of the folds in the stomach and

efferent loop, and the roentgenologic diagnosis of gastrojejunitis, in experienced hands, is usually reliable. Apparently the most reliable roentgenoscopic evidence is that in which the inflammatory process was sufficiently extensive to give rise to gross defects. The question naturally arises as to how often gastric disturbances are the result of patchy or diffuse inflammatory states unrecognized in the absence of roentgenographic findings and in the absence of routine gastroscopic study. The gastroscopic appearance of the stomach in various forms of gastritis is instructively portrayed in the monographs or atlases of Schindler, Henning, and Moutier.

It is unfortunate that gastroscopy is such a highly technical procedure. In unskilled hands it is also a dangerous one. The circumspect physician cannot escape the conviction at times that some pathologists, gastroscopists and even roentgenologists or other protagonists of gastritis as an important entity, are unduly imbued with an enthusiasm comparable to that displayed on occasions by certain allergists and endocrinologists. One also gets the impression that the enthusiastic gastroscopist finds some abnormality of the gastric mucosa, to which he attaches undue significance, in the majority of cases in which he makes an examination. In this respect Katsch himself has pointed out the fallacy of a diagnosis made exclusively from the results of gastroscopic examination because, "a clear relation between gastroscopic findings and the clinical picture, even excluding everything but the subjective illness, can be established only in clear-cut cases with any degree of certainty."

The necessity for careful appraisal of all the facts, subjective and objective, as in other phases of medicine, is obvious. Careful teamwork among clinician, laboratory worker and surgeon is often essential in order that diagnostic and therapeutic problems in this field may be successfully surmounted.

G. E.

REVIEWS

The Normal Diet and Healthful Living. By W. W. SANSUM, R. A. HARE, and R. BOWDEN. 243 pages; 12 × 22 cm. Macmillan Company, New York. 1936. Price, $2.00.

This is a book intended for popular appeal, written by the authors to present in a permanent form, especially for their own patients, facts of general health interest. A bird's eye view is given of such topics as the elements of nutrition, the vitamins, the physiology of digestion, the "elimination of wastes," and many familiar medical disorders including indigestion, allergy, underweight and overweight and the care of teeth. Finally, there is a brief discussion of bacteriology, especially as it relates to focal infection, with particular emphasis upon the work of Dr. E. C. Rosenow. The material which has been mentioned occupies the first 186 pages of the book. The remainder is taken up with the customary appendices to be found in such treatises, including a few words on menu planning, followed by the usual sample menus, food tables, and weight tables.

G. A. H.

A Textbook of Obstetrics for Students and Practitioners. By FREDERICK C. IRVING, A.B., M.D., F.A.C.S. 558 pages; 24 × 15.5 cm. Macmillan Company, New York. 1936. Price, $6.00.

Good textbooks on obstetrics are always timely. By sound conservative advice they advance the efforts of the profession to reduce maternal mortality.

In elaborating the outlines used in the teaching of students in the Harvard Medical School, the author has created a clear and useful textbook. In keeping with the avowed purpose of making the book concise, the author has intentionally avoided the history of obstetrics, and the presentation of all sides of controversial subjects, and frankly states that the work does not cover the entire field. The contents are discussed under the conventional headings, and the index is ample. With the exception of the roentgenogram reproductions, which for the most part are only fair examples of the subjects which they are intended to illustrate, all of the 357 illustrations are clear outline drawings many of which have been modified from other works to which due credit is given. Attention is called to the excellent bibliography to be found at the end of each chapter which should prove invaluable to students and practitioners using this book as a guide. The pathologic descriptions are thorough.

The author prefers pentobarbital and scopolamine as analgesic agents during labor and uses rectal ether to control excitement. The toxemias of late pregnancy are classified as preëclampsia and eclampsia. Gynoplastic repairs following delivery are definitely frowned upon as is also the so-called "prophylactic forceps" operation. One cannot but feel that the descriptions of operative procedures are given too much space, and that prenatal and postnatal care should be given more emphasis in any work intended for the student and practitioner.

The author states that the book represents the policies and practice of the Boston Lying-In Hospital, and from it we learn that such obstetrical complications as septic abortion, placenta previa, premature separation of the normally implanted placenta, and eclampsia are treated conservatively in that clinic. Of especial interest to the readers of this journal are the discussions of the medical complications of pregnancy. These are brief but give concisely the author's viewpoint as an obstetrician on such questions as the indications for the termination of pregnancy.

The book is well written, and since it presents the author's vast experience in obstetrics in a readable form, it should prove of definite value to the student and practitioner to whom it is warmly recommended.

J. E. S.

The Bacteriology of Typhoid, Salmonella and Dysentery: Infections and Carrier States. By LEON C. HAVENS, M.D., Director of Laboratories, Alabama State Department of Health. First Edition. 158 pages. The Commonwealth Fund, 41 East 57th St., New York City.

This small volume sums up certain investigations and experiences of the author while actively engaged in public health work in the field and laboratory. In thirteen short chapters, each with its summary and bibliography, the more important characteristics of the intestinal bacteria are discussed and selected laboratory methods described. Clinical bacteriologists will find the book of especial interest. A sense of undue brevity and of incompleteness in some of the chapters may be explained by the fact that the work was posthumously published.

S. L. J.

Examination of the Patient and Symptomatic Diagnosis. JOHN WATTS MURRAY, M.D. Second Edition. 1219 pages. C. V. Mosby Co., St. Louis. 1936. Price, $10.00.

This work is an effort to present, in minute detail, the procedure for obtaining a clinical history and performing a physical examination. The book is divided into two sections, the first on history taking and general physical examination; the second on specific symptoms and physical signs of disease localized in organs or body parts.

After a long introduction, the author presents an outline of history and physical examination, then proceeds to an extremely minute analysis of history taking, given in catechism, or question and answer form. The answers are frequently cast in the shape of lists of diseases which may be related to certain conditions; an unfortunate method, since the lists are so long as to make this section almost unreadable.

Many statements are introduced as facts which do not bear up under analysis. For example, in the section on Past History, question five—"Has the patient ever had diabetes?"—is answered thus, "Pulmonary tuberculosis is perhaps the most frequent complication in consequence of diabetes, the diabetic state following its development." . . . Question eight: "Patient ever had chlorosis or anaemia?" Answer: "Chlorosis may give rise to gastric ulcer, exophthalmic goiter, amenorrhea." . . . On Page 68: "Cardiac hypertrophy, cardiac valvular disease, atheromatous degeneration of the arteries, and aneurysm may cause hemorrhagic neuroretinitis." Page 70: "Floating kidney may cause dilatation of the stomach." These, and many other similar statements, are offered without explanation or qualification.

In the second section diseases of specific parts or tracts of the body are considered. Each division is preceded by some details of history and physical examination, again in question and answer form, with the answers suggesting the disease possibilities. The reader is evidently expected to refer to the paragraphs describing those diseases, although specific references are not given. Many of the disease descriptions are very good, especially those of the respiratory tract. On the other hand, several very important ones are apparently missing entirely. The index, for example, does not list lobar pneumonia, typhoid fever, or pernicious anemia, although these diseases are mentioned at times in the text.

The reviewer doubts if this book could be of much help unless it were used simply as an aid to other texts. Many suggestions in it are very helpful, but as a whole, it would be improved by condensation and rearrangement.

T. N. C.

Collected Writings of ALFRED F. HESS with biographical memoir and bibliography. 2 volumes, cloth, 1453 pages, illustrated. Charles C. Thomas, Baltimore. 1936. Price, $15.00.

The more important scientific contributions of Alfred Fabian Hess have been collected, edited and published in two well bound, well printed volumes. Abraham Flexner wrote an appreciative and interesting biographical memoir which precedes the writings. In this sketch are traced the main events of Hess' life and the principle influences which shaped it. It contains as well a critical appraisal of his work as a scientist and investigator and the place he holds in pediatrics.

The collected papers represent some of the most important investigative work done in medicine during the first third of this century. Such broad topics as tuberculosis in infancy, the antiscorbutic vitamin and infantile scurvy, and the effect of irradiation of foodstuffs are discussed in the reports of numerous investigations. One is impressed at how much pioneer work this man did and how many accepted and well trod avenues of medical thought were either indicated or opened up by his researches. In addition to the above mentioned investigations there are papers on rickets, purpura, alimentary intoxication and various other pediatric problems. It is characteristic of these articles that they are short, well written and easy to understand. His complete bibliography is appended to the work.

In summing up Hess' position Dr. Edwards A. Park writes, "Dr. Hess was the foremost investigator among pediatricians in this country." . . . "A great skirmisher on the forefront of scientific progress, with an almost uncanny eye for the point at which the next attack should be made, with a genius for predicting the course which investigation should take, with almost infallible judgment on the basis of slight evidence and simple experiment as to where the weak point in the armor of ignorance lay." . . . "Hess was the best example of what can be accomplished in science by the ability to think alone and unaided."

These volumes are a valuable addition to the library of any one interested in medical and pediatric progress.

T. C. G.

COLLEGE NEWS NOTES

Gifts to the College Library

Acknowledgment is made of the following gifts received recently for the Library of the American College of Physicians from the authors:

Dr. Percy Brown (Fellow), Boston, Mass.—1 autographed book, "American Martyrs to Science Through the Roentgen-Rays";
Dr. George B. Eusterman (Fellow), Rochester, Minn.—1 autographed book (with Dr. Donald C. Balfour), "The Stomach and Duodenum";
Dr. Frederick T. Lord (Fellow), Boston, Mass.—1 autographed book, "Lobar Pneumonia and Serum Therapy";
Dr. Herman O. Mosenthal (Fellow), New York, N. Y.—1 autographed book, "The Diagnosis and Treatment of Variations in Blood Pressure and Nephritis";
Dr. William M. LeFevre (Fellow), Muskegon, Mich.—2 reprints;
Dr. Lewis J. Moorman (Fellow), Oklahoma City, Okla.—3 reprints;
Dr. Joseph M. Perret (Fellow), New Orleans, La.—13 reprints;
Dr. Maxim Pollak (Fellow), Peoria, Ill.—1 reprint;
Dr. William B. Rawls (Fellow), New York, N. Y.—3 reprints;
Dr. Martin J. Synnott (Fellow), Deceased—1 reprint;
Capt. Elbert DeCoursey (Associate), M.C., U.S.A.—1 reprint;
Dr. Harold R. Keeler (Associate), Philadelphia, Pa.—5 reprints;
Dr. Arthur R. Masten (Associate), Wheat Ridge, Colo.—5 reprints.

Dr. Edward L. Turner (Fellow), from 1931 to 1936 associate professor and professor of internal medicine, American University of Beirut, Beirut, Syria, has recently accepted the appointment of professor of medicine and head of the division of medicine at Meharry Medical College, Nashville, Tenn. He will spend his full-time with the work of the college and hospital in connection with the reorganization of the division of medicine.

Dr. Ralph M. Fellows (Fellow), for sometime connected with the Menninger Clinic at Topeka, Kan., has accepted the superintendency of the Osawatomie State Hospital, Osawatomie, Kan.

The Washington Society of Pathologists has elected the following officers for the coming year: Dr. Roger M. Choisser (Fellow), President; Capt. Elbert DeCoursey (Associate), M.C., U. S. A., Secretary-Treasurer.

Dr. Matthew Shapiro (Associate), New York City, has been appointed assistant professor of clinical medicine in Columbia University College of Physicians and Surgeons.

Dr. R. H. Kampmeier (Fellow), has left Louisiana State University Medical Center to accept an appointment at Vanderbilt University School of Medicine, Nashville, Tenn.

Dr. George A. Gray (Associate), formerly of Abilene, Tex., has become Director of the Nolan County Health Unit, Sweetwater, Tex.

Dr. John H. Musser (Fellow), New Orleans, La., was the guest clinician on the program of the Post-Graduate Assembly of the North Carolina State Medical Society at Banner Elk, N. C., August 20 to 21. The Post-Graduate Assembly is conducted on "Internal Medicine and Therapeutics."

The Committee on Arrangements included Dr. R. H. Hardin (Fellow), Banner Elk, N. C., Chairman; Dr. C. L. Sherrill (Fellow), Statesville, N. C.; and Dr. James W. Vernon (Fellow), Morganton, N. C.

Dr. Wingate M. Johnson (Fellow), Winston-Salem, N. C., President-Elect of the North Carolina State Medical Society, delivered an address on "My Experience with Influenza"; Dr. Verne S. Caviness (Fellow), Raleigh, N. C., "Pneumonia"; Dr. C. H. Cocke (Fellow), Asheville, N. C., Governor for North Carolina and Chairman of the Board of Governors, "Evolution of the Modern Treatment of Tuberculosis"; Dr. D. W. Holt (Fellow), Greensboro, N. C., "Backache." Dr. L. B. McBrayer (Fellow), Southern Pines, N. C., Secretary and Treasurer of the North Carolina Medical Society, and also Dr. Musser presented addresses on the evening of the banquet.

Dr. George R. Minot (Fellow) and Dr. C. Sidney Burwell (Fellow), Dean of Harvard Medical School, were among those who addressed the Boylston Medical Society, on the occasion of its one hundred and twenty-fifth anniversary recently. The Boylston Medical Society is probably the oldest students' medical school organization in America. The dinner was held at the Harvard Club. Dr. Burwell is President-Elect of the Society.

Dr. William G. Herrman (Fellow), Asbury Park, N. J., has been advanced from 1st Vice-President to President-Elect of the Medical Society of New Jersey. Dr. Francis R. Haussling of Newark, who was installed as President, resigned because of ill health, whereupon Dr. Spencer T. Snedecor of Hackensack, President-Elect, was advanced to the Presidency and Dr. Herrman to the post of President-Elect.

Dr. Warren Coleman (Fellow), New York City, is one of the Vice-Presidents of the Physicians' Home, which has been recently reorganized and which now plans a vigorous campaign to finance a permanent home for aged and infirm physicians.

Dr. Guy C. Jarratt (Associate), Vicksburg, Miss., has been reëlected Secretary of the Mississippi State Pediatric Society.

Dr. J. Arthur Myers (Fellow), Minneapolis, Minn., and Dr. Samuel H. Snider (Fellow), Kansas City, Mo., are Vice-Presidents of the newly formed American Academy of Tuberculosis Physicians.

Dr. Andrew C. Ivy (Fellow), Chicago, has been elected Vice-President of the Chicago Society of Internal Medicine.

Dr. Mark S. Knapp (Fellow), Ann Arbor, Mich., has announced his resignation as executive secretary and director of medical research of the Rackham Fund, Detroit, a position he has held since the fund was created in 1934.

Dr. John D. Dunham (Fellow), Columbus, Ohio, has been appointed to the city board of health, succeeding the late Dr. Wells Teachnor, Sr.

Dr. Charles E. Sears (Fellow), Portland, Ore., has been made President-Elect of the Pacific Northwest Medical Association.

Dr. Clayton E. Royce (Fellow), Jacksonville, Fla., has been elected a Vice-President of the Chattahoochee Valley Medical Association.

Dr. Anthony Bassler (Fellow), New York City, and Dr. Martin E. Rehfuss (Fellow), Philadelphia, have been appointed President and Vice-President, respectively, of the American delegation to the International Congress on Hepatic Insufficiency in Vichy, France, September 16 to 18, 1937.

Dr. Newton G. Evans (Fellow) is President of the Los Angeles Cancer Society.

The pathology laboratory of Beth Israel Hospital has been dedicated in honor of Dr. Isidore W. Held, clinical professor of medicine at New York University College of Medicine, the dedication ceremonies taking place on Dr. Held's sixtieth birthday. Among speakers at the dedication was Dr. John Wyckoff (Fellow), dean of New York University College of Medicine.

The sixty-sixth annual session of the Colorado State Medical Society was held at Glenwood Springs, September 9 to 12. Aside from the regular program, there was a presentation of the past presidents of the Society, in the order of their seniority. Dr. Hubert Work (Fellow), Englewood, Colo., former President of the American Medical Association and Secretary of the Interior under President Coolidge, was presented as the senior living president of the Society. The banquet was dedicated to Dr. Josiah N. Hall (Fellow), Denver, for several years the Colorado Governor for the American College of Physicians, in recognition of his fiftieth year of attendance at the annual meetings of the Society. Dr. Hall has been a member of the Society fifty-two years. He has been a president of the State Society, of the State Board of Health and of the State Board of Medical Examiners. He has served on the Judicial Council of the American Medical Association and has been a member of the House of Delegates at various times. Dr. Hall has been professor of medicine at the University of Colorado School of Medicine for many years.

Dr. Guy H. Turrell (Fellow), Smithtown Branch, N. Y., is Secretary of the New York State Sanitary Officers' Association, the name of which has recently been changed to the New York Health Officers' Association.

Dr. Wade W. Oliver (Fellow), professor of bacteriology, Long Island College of Medicine, Brooklyn, has been elected Secretary of Health Research, Inc., a non-profit corporation recently formed by the New York City Department of Health to accept and administer funds offered for financing research in the city's laboratories. The department plans to open a convalescent serum center.

Dr. Henry M. Moses (Fellow), Brooklyn, is the director of the medical service of the new Brooklyn Cancer Institute, opened at Kings County Hospital during September, as an independent clinical unit of the division of cancer of the city department of hospitals. Surgical and radiotherapy services under individual directors have also been established. The three directors will be responsible for clinical policy in general and for the treatment and care of patients individually. The institute is under the general administrative supervision of the medical superintendent of Kings County Hospital. There is a visiting staff of thirty-one physicians. Beds are to be used as far as possible for cases of doubtful classification and for recognized tumor cases requiring short hospitalization, in order that the patients still reclaimable may find facilities for care.

Dr. William V. Wilkerson (Fellow), Highcoal, W. Va., is president of the Boone County (W. Va.) Medical Society.

Dr. Daniel L. Finucane (Associate), formerly of Glenn Dale, Md., has been appointed associate professor of clinical medicine at Georgetown University School of Medicine, Washington, D. C.

Dr. J. P. Bowdoin (Fellow), Atlanta, Ga., has been elected Secretary-Treasurer of the Georgia State Child Health and Welfare Council.

Dr. Leon S. Lippincott (Fellow), Vicksburg, Miss., has been elected Secretary-Treasurer of the Mississippi State Hospital Association; Dr. Lippincott is also Secretary of the Mississippi State Charity Hospital at Vicksburg.

Dr. Franklin B. Bogart (Fellow), Chattanooga, Tenn., has been elected Secretary-Treasurer of the Tennessee Radiological Society.

The Texas State Heart Association has elected the following officers for the coming year: Dr. Edward H. Schwab (Fellow), Galveston, President; Dr. George R. Herrmann (Fellow), Galveston, Vice-President; Dr. Robert M. Barton (Fellow), Dallas, Secretary.

Dr. John G. Young (Fellow), Dallas, Tex., is Vice-President of the Texas Pediatric Society for the coming year.

Dr. Walter B. Martin (Fellow) and Dr. Frank H. Redwood (Fellow), both of Norfolk, have been elected President and President-Elect, respectively, of the Norfolk County (Va.) Medical Society for the coming year.

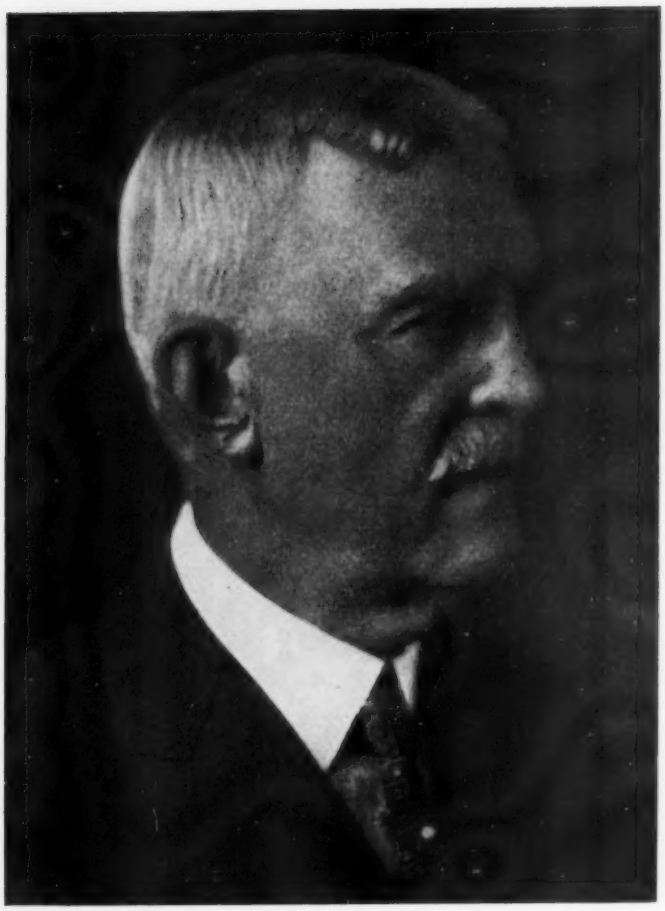
Dr. Frank C. Hodges (Fellow), Huntington, W. Va., has been elected a Vice-President of the West Virginia State Medical Association.

Under the Presidency of Dr. David Riesman (Fellow), Philadelphia, the Interstate Postgraduate Medical Association of North America is holding its International Assembly for 1936 at St. Paul, October 12 to 16.

Dr. W. A. Dearman (Fellow), formerly of Gulfport, Miss., has been appointed assistant superintendent of the Mississippi State Hospital at Whitfield.

Dr. W. M. Sheppe (Fellow), Wheeling, W. Va., has been elected Secretary of the Ohio County (W. Va.) Medical Society for the coming year.

Dr. Martin E. Rehfuss (Fellow), Philadelphia, clinical professor of medicine at Jefferson Medical College of Philadelphia since 1933, has been promoted to professor of clinical medicine.



With warmest regards of your friend
J. H. Sudrow
November 29th '29.

OBITUARIES

DR. JAMES MESCHTER ANDERS

James Meschter Anders, M.D., Ph.D., LL.D., Sc.D., the Nestor of Philadelphia's medical profession, the first Master of the American College of Physicians and its President during 1922–23, died at his summer home at Bluehill Falls, Maine, on August 29, 1936; aged 82.

Dr. Anders was born in Fairview Village, Montgomery County, Pa., on July 22, 1854, and received his education in the public schools of Norristown, Pa., and at the theological seminary, under the auspices of the Mennonite Church, at Wadsworth, Ohio. In 1877, he graduated from the University of Pennsylvania School of Medicine and in the same year received his degree of Doctor of Philosophy.

He served his internship at the Episcopal Hospital, Philadelphia, and, in 1888, became visiting physician to the same institution. One year later Dr. Anders was appointed visiting physician to the Medico-Chirurgical Hospital and in the same year was made a member of the visiting staff of the Philadelphia General Hospital.

In 1889, Dr. Anders became a lecturer on Materia Medica at the Medico-Chirurgical College, and one year later was elected Professor of Hygiene and Pediatrics. In 1891, Dr. Anders became Professor of the Theory and Practice of Medicine and Clinical Medicine in the Medico-Chirurgical College, a position he held with credit and honor for over twenty-five years. Dr. Anders was the author of a textbook known as the "Principles and Practice of Medicine," which passed through fourteen editions, and he was co-author of a "Text Book of Medical Diagnosis."

Dr. Anders was a frequent contributor to medical literature throughout his long and distinguished career, over a hundred scientific articles being listed from his pen. He was widely and favorably known as a conservative and helpful consultant by the medical profession, and his services were sought by practitioners, both at home and at distant points.

Dr. Anders was greatly interested in educational and civic problems afield from medicine and, at the time of life when many physicians become both formalized and even crystalized in thought, possessed a clarity and breadth of vision inspiring to all who were fortunate enough to come into contact with him.

Dr. Anders was much interested in Preventive Medicine and advanced its interests by practical application of sound principles as well as by well thought out addresses before influential professional and lay groups.

In 1923, he was made a Chevalier of the Legion of Honor of France and, in 1928, had the honorary degree of Sc.D. conferred upon him by his Alma Mater, the University of Pennsylvania. Many other well deserved honors, medical, civic and national, were bestowed upon Dr. Anders, but he

remained, as in the beginning, modest, unselfish, altruistic, and was possessed by an admirable desire to prove useful to his profession, his patients and to the general public weal.

The American College of Physicians was very dear to the heart of Dr. Anders and he devoted much time and thought to how this organization could best advance and uphold the interests of the medical profession and the public the profession serves.

Dr. Anders' death has caused the College to lose a much admired and beloved Master, the medical profession a skilled and devoted practitioner, and the world has lost a man of exemplary character who spent his long life in attempting to make the problems of others less difficult.

E. J. G. Beardsley, M.D., F.A.C.P.,
Governor for Eastern Pennsylvania.

DR. EDWARD GILMER THOMPSON

Dr. Edward Gilmer Thompson (Fellow), Memphis, Tennessee, died June 21, 1936; aged 52 years.

Dr. Thompson was born in Louisa, Virginia, August 29, 1884, and in his early years his family moved to Marianna, Arkansas, where he resided until he came to practice his profession in Memphis in 1913.

He secured his preliminary education in the public schools of Marianna and later attended the Branham and Hughes Preparatory School. He received the degree of Bachelor of Arts at Vanderbilt University in 1907 and his medical education was obtained at the University of Pennsylvania from which he graduated with honors in 1911. He was a member of the Phi Delta Theta, Alpha Kappa Kappa and Alpha Omega Fraternities.

Following his graduation in medicine he served a two year internship at the Episcopal Hospital in Philadelphia, Pennsylvania, and in 1913 began the practice of medicine in Memphis, Tennessee. He devoted his professional career to internal medicine, was a Fellow of the American College of Physicians and Associate Professor of Medicine at the University of Tennessee College of Medicine, held staff positions at the Methodist and John Gaston Memorial Hospitals and was on the staff of the Illinois Central Railway System.

In 1917 he was among the first to offer his services to his country in the great war. With the rank of Captain in the Medical Corps he was a member of Hospital Unit P and for fourteen months was attached to Base Hospital 15 at Chaumont, France. Though quiet and unobtrusive Dr. Thompson took an active interest in organized medicine, being a member of the Memphis and Shelby County Medical Societies, Tennessee State Medical Association, The American Medical Association and the Southern Medical Association.

Edward Thompson was not only much beloved by a large clientele but he was a doctor's doctor, being the personal physician probably of more of

the Memphis medical profession than any other member of it. His strong sense of fidelity to his patients doubtless shortened his life. His personal traits of character were outstanding. Clean in word and thought and deed, faithful, conscientious and loyal to his high conception of his duty, no one ever heard a harsh or unkind word spoken of him. He was loved and deservedly trusted implicitly by everyone who knew him. Competent, dependable, wholly trustworthy, the profession in Tennessee can ill afford to lose him.

J. Owsley Manier, M.D., F.A.C.P.,
Governor for Tennessee.

DR. JAMES FRANKLIN ACKERMAN

Dr. James Franklin Ackerman (Fellow), Asbury Park, N. J., one of six sons of Joseph and Susan Ackerman, was born in Nashua, N. H., December 29, 1864. He received his preliminary education at Francestown Academy in New Hampshire and in the public schools of Shelburn Falls, Mass. He received a portion of his college training at Amherst College, followed by his medical training at the New York Homeopathic College, New York City, graduating in 1890. Thereafter he immediately went to Asbury Park, where he resided until his death on August 5, 1936. He was associated with his late brother, Dr. Joseph Ackerman, who died about a year ago.

Dr. Ackerman was highly regarded as a citizen in Asbury Park and was affectionately referred to as the " father " of two different hospitals, and at the time of his death was chief of staff of the Ann May Hospital, Spring Lake, and of the Fitkin Memorial Hospital, Neptune, which succeeded it. He was ex-president of the Asbury Park Medical Society, the Monmouth County Medical Society and the New Jersey State Homeopathic Society. He was an active member of the New Jersey State Medical Society, the New York Academy of Medicine and the American Medical Association. He had been a Fellow of the American College of Physicians since 1931.

Dr. Ackerman is survived by his second wife, Mrs. Anna Rouse Ackerman; a brother, George, of Nashua, N. H.; and three daughters, Mrs. James A. Fisher, Mrs. Frank W. Cole and Mrs. O. K. Parry, all of Asbury Park.

Both the College and the medical profession have suffered a great loss in the death of this valuable member.

Clarence L. Andrews, M.D., F.A.C.P.,
Governor for New Jersey.

DR. SIDNEY KOHN SIMON

" Sidney Kohn Simon: born, New Orleans, La., January 25, 1878; A.B., 1899, Tulane University College of Arts and Sciences; M.D., 1903, Tulane

University of Louisiana Medical Department; visiting physician, 1905–12, Charity Hospital, New Orleans; visiting physician, 1905 to date, and chief of Gastro-Intestinal Department, 1920 to date, Touro Infirmary; professor of gastro-enterology, Tulane University of Louisiana School of Medicine; member and ex-member of council, American Gastro-Enterological Association; member and ex-president, Southern Gastro-Enterological Association; ex-secretary and ex-member of council, American Society of Tropical Medicine; ex-secretary and ex-chairman of the Section on Gastro-Enterology, and Fellow, American Medical Association; member, Southern Medical Association and Southern Gastro-Enterological Club; Fellow of the American College of Physicians since 1928."

Dr. Simon has for years been regarded as an outstanding leader in his chosen specialty, gastro-enterology.

His contributions to the literature of this field of medicine have been too numerous to mention at this time. Suffice it to say that the influence of his writing and clinical teaching constitutes a living and lasting monument to his memory in the minds and hearts of the medical profession.

J. E. KNIGHTON, M.D., F.A.C.P.,
Governor for Louisiana.